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The Bancroft Memorial Lecture.[1]

SOME RECENT WORK ON HYPERTENSION.[1]

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A GOOD measure of Bancroft's intellectual stature is that he was equally outstanding in observation and in experiment. It was observation that linked his name with filariasis, and the best known instance of his experimental ability was the work which led to the founding of the dried beef industry in Queensland and which has recently been extended to many other biological products. In this connexion it may be noted that dried human serum, which has recently found a place in therapeutics, is a lineal if somewhat refined descendant of Bancroft's pemmican. Thus time has paid a graceful compliment to one whose curiosity was not limited by his professional horizon.

The term "Bright's disease" covers a wide variety of disorders, in which two distinct morbid processes—namely, renal damage and hypertension—are interwoven to a most confusing extent. This confusion is well reflected in the history of the disease during the past century. Thus for many years after Bright's observation of the close relationship existing between nephritis and cardiac hypertrophy, it was widely assumed that a raised blood pressure implied incurable renal disease. And when Clifford Allbutt,[(1)] seventy years later, described hypertensive patients who remained free from renal symptoms, even after many years, it was generally believed that no sufferer from this primary hypertension (hyperpiesia, essential hypertension) ever succumbed to renal failure. This error was in turn corrected by Volhard and Fahr,[(2)] who showed that some hyperpietics develop early and fatal renal insufficiency (malignant hypertension); but after thirty years this conception is still not universally accepted. It now seems that history is repeating itself, for many writers have inferred from Goldblatt's work that all hypertension is renal in origin, a view which I believe to be unwarranted. But if the wheel has turned a full circle, it has all the time been slowly rolling forward, and my purpose is to show that we are now in a position to attempt some sort of integration of the problem of Bright's disease and hypertension.

The key to the problem is the syndrome of malignant hypertension—that is, a form of primary hypertension which occurs in relatively young subjects and leads to early death from renal incompetence. The reluctance in some quarters to accept this conception has been well grounded. In the first place, impairment of renal function appears so early that its symptoms are generally present when the patient first seeks medical advice. Secondly, the symptoms and signs of the disease are not uncommonly found in the later stages of any kind of renal disease complicated by hypertension. Thirdly, the final histological picture of "chronic interstitial nephritis" is likewise found in other hypertensive diseases. And, finally, this picture is one which the pathologist, on general grounds, has often regarded as inflammatory in nature. There were, therefore, good arguments against the conception that malignant hypertension is a form of essential hypertension.

Further study was made possible by the work of Goldblatt and his associates.[(3)] Goldblatt constricted the renal arteries of the dog by an adjustable metal clamp, and so produced a form of hypertension resembling in all important points the disease as it occurs in man. This work opened up a wide field of research, and amongst other things it gave the student of Bright's disease an opportunity of discovering, by experiment, exactly what damage hypertension can cause in the kidney. The opportunity was not neglected. It was soon found by Goldblatt, and

[1] Delivered before the Queensland Branch of the British Medical Association on June 4, 1943, at Brisbane.

independently by Wilson and Pickering,[5] that in some hypertensive animals vascular lesions developed, identical with those found in malignant hypertension. These lesions consisted of an acute necrosis of the wall of isolated small arteries, the dead wall becoming soaked with fibrin and blood ("necrotizing arteritis"), and in other vessels, a conspicuous form of intimal thickening, composed of delicate, almost myxomatous connective tissue and termed, not very aptly, "*endarteritis fibrosa*". These vascular lesions were scattered widely through the body, especially in the splanchnic region, but they were absent from the kidneys. It was concluded that the lesions were the result of hypertension, from the effects of which the kidneys were protected by the barriers afforded by the clamps. Goldblatt, however, pointed out that the lesions occurred only when the clamps were applied tightly enough to cause, not only high blood pressure, but also impairment of renal function, and he concluded that renal failure, as well as hypertension, was concerned in the production of the lesions. This interpretation was perhaps justified on the evidence then available; but the implication that renal failure plays some part in causing malignant hypertension was not in harmony with the clinical conception of this disease. Meanwhile it had occurred to Dr. Clifford Wilson that further evidence might be obtained by constricting one renal artery and leaving the opposite kidney and its vessels intact. The presence of one normal kidney would be useful for two reasons: it would give reasonable certainty that renal failure could not be blamed for any lesions, which might be found; and it would provide an opportunity to study the effect of hypertension on an intact kidney. Wilson and I had for some years collaborated in experimental work on rats, and it was decided to adapt Goldblatt's technique to this animal. I should mention here that I had at this time only a superficial knowledge of Bright's disease, and that the interpretation of our results has been essentially the work of Dr. Wilson and of Professor Ellis, in whose nephritis clinic at the London Hospital the work had its origin. We were not at first hopeful of positive results, since Goldblatt and others had found that in the dog the unilateral operation caused only a transient hypertension. However, we were more fortunate, for we found that a considerable proportion of rats developed apparently permanent hypertension. These hypertensive rats were killed at varying intervals and the tissues were prepared for microscopic examination.

The Effect of Acute Hypertension on the Intact Kidney and Other Tissues.

In those rats which were killed after hypertension had persisted for short periods—that is, from a few days to several weeks—the acute vascular lesions described earlier were found in various organs, notably the pancreas, the intestine and the heart, where small flame-shaped hæmorrhages were often visible under the pericardium.[6] No such lesions were found in the "clamped" kidney, in which merely a variable degree of symmetrical atrophy was found, with occasional partial infarction. In the opposite (or "unclamped") kidney lesions typical of malignant hypertension were found. These included fibrinoid necrosis of the afferent glomerular arterioles (Figures I and II), *endarteritis fibrosa* of larger vessels (Figures III and IV), and a variety of acute glomerular lesions ranging from focal necrosis (Figures V and VI) of the tuft with adhesion to the parietal layer of Bowman's capsule, to complete hæmorrhagic infarction. In some of the neighbouring tubules atrophy and dilatation were present, and slight inflammatory reaction was visible in the supporting tissue. It was inferred from these findings that the lesions in the "unclamped" kidney were the result of hypertension and that renal failure played no part in their production. These lesions are identical with those found in malignant hypertension in man, and our findings therefore lend direct support to the view that malignant hypertension is a form of primary or essential hypertension. It was pointed out that, since the lesions, like the clinical characters, of malignant hypertension are commonly found in other forms of chronic hypertensive disease, these lesions must be regarded as expressions of raised blood pressure as such, and not as being peculiar to any one disease. To avoid confusion it was suggested, however, that the term "malignant hypertension" should be restricted to its present usage—that is, to the malignant form of essential hypertension.

The Effect of Chronic Hypertension.

In a second series of experiments,[6] the animals were not killed until hypertension had persisted for several months. The histological changes in these animals were more chronic and more widespread. In the "unclamped" kidney, inspection of the glomeruli revealed varying degrees of hyalinization of the tuft and obliteration of the capsular space (Figures VII and VIII). Many glomeruli were reduced to structureless hyaline spheres, and glomerular counts indicated that some had completely disappeared. The convoluted tubules in some areas were widely dilated and full of eosinophilic colloid. In other areas the tubules were atrophied, consisting of shrunken epithelial cells on a thickened basement membrane. There was also gross fibrosis of the interstitial tissue, the kidney in some instances appearing granular to the naked eye. The renal arteries were also abnormal. Medial hypertrophy was conspicuous (Figure IX) and was accompanied in some cases by a fibrous thickening of the intima containing newly formed elastic tissue. In other small arteries irregular scarring with loss of muscular tissue and distortion of the elastic lamellæ were apparent—changes which apparently represent the healed stage of necrotizing arteritis. In some rats acute vascular and glomerular lesions were present as well as these more chronic changes. The changes were focal in distribution; but in the more severe grades very little normal tissue remained. None of the foregoing lesions were observed in the "clamped" kidney, which was generally moderately or severely atrophied and was in some instances reduced to a calcareous nodule.

Acute and chronic vascular lesions were present in other organs, especially the pancreas, the intestine and the heart. Leaf-shaped pearly scars were commonly visible under the pericardium, and left ventricular hypertrophy was conspicuous. In some instances a clear effusion was observed in the serous cavities and between the layers of the mesentery. It is not clear whether this effusion was related to local vascular lesions or to cardiac failure.

The absence of medial hypertrophy in the vessels of the "clamped" kidney provided strong evidence that the clamp had in fact acted as a barrier against the raised blood pressure, and it seems clear that the chronic lesions in the "unclamped" kidney and in other tissues are, like the acute lesions, directly attributable to hypertension. These renal changes bear close comparison with the histological picture of "chronic interstitial nephritis", which is found *post mortem* in malignant hypertension and also in many other forms of chronic hypertensive renal disease, and which has in the past been widely regarded as inflammatory in nature.

The Vicious Circle in Bright's Disease.

It is a well-known fact that a wide variety of diseases involving extensive disorganization of the architecture of the kidney are complicated by secondary hypertension, which in the light of Goldblatt's work may reasonably be attributed to renal ischæmia. The question arises, therefore, whether the damage inflicted on the kidney by hypertension itself is similarly capable of generating further hypertension. Some of the vascular lesions in the hypertensive rat, particularly *endarteritis fibrosa*, are characterized by a pronounced narrowing of the lumen, which would be expected to have the same effect as a clamp.

Our final series of experiments was designed to obtain more direct evidence on this point by excision of the "clamped" kidney at various intervals after the onset of hypertension. Our results showed that recent hypertension was always promptly abolished by this operation. In some animals with more chronic hypertension the blood pressure also returned to normal after nephrectomy, and in such instances subsequent post-mortem examination generally revealed little or no evidence of hypertensive injury in the remaining kidney. In other rats, however,

removal of the "clamped" kidney failed to abolish the hypertension, and in these animals examination of the remaining kidney invariably revealed extensive chronic hypertensive disease. In some animals, moreover, acute vascular and glomerular lesions were observed many weeks after removal of the "clamped" kidney. Thus a high blood pressure capable of causing further renal damage may persist after the primary cause of the hypertension has been removed, but only in the presence of extensive injury to the "unclamped" kidney. It seems probable, therefore, that this residual or secondary hypertension is generated in the remaining kidney, and this finding provides strong experimental support for the occurrence of a vicious circle in hypertensive renal disease in man. This conception accounts for the rapidly progressive course of malignant hypertension and also for the malignant termination which is sometimes observed in other forms of chronic hypertensive renal disease.

We had hoped to obtain further evidence on this subject and also to follow the vicious circle to its logical end; but unfortunately all our laboratory animals were destroyed at the outbreak of war.

Before we consider the clinical implications of these experiments, it is necessary to mention that Schroeder and Neumann[7] have repeated our experiments on rats and have stated that acute vascular lesions commonly appear in the "clamped" as well as in the "unclamped" kidney. Our finding that the "clamped" kidney remained free from such lesions is nevertheless corroborated by the results obtained by Wilson and Pickering[4] on the rabbit, and by Goldblatt[3] on the dog. The discordant results of Schroeder and Neumann are possibly related to their use of ligatures and not clamps to compress the artery. Wilson and I abandoned ligatures at an early stage of our experiments. It is not easy to produce by ligature graduated constriction of a vessel, the diameter of which is of the order of one millimetre, and the barrier is neither so rigid nor so permanent as that afforded by a metal clamp. Once the vicious circle has become established, relaxation of the ligature will expose the "clamped' kidney to the effects of secondary hypertension. Wilson and I have, in fact, observed that hypertensive lesions appear in the "clamped" kidney if the clamp is removed from rats showing secondary hypertension. In the experiments of Schroeder and Neumann the frequent appearance of muscular hypertrophy in the vessels of the "clamped" kidney strongly suggests that the ligature had failed to afford a permanent barrier against the raised tension. Whether this is the true explanation or not, the point is vital to our thesis, and independent investigation is clearly desirable.

Clinical Implications.

The Cause of the Confusion in Bright's Disease.

It has long been appreciated that a major obstacle to the classification and understanding of Bright's disease is the observation that conditions so widely separated as malignant hypertension, true primary nephritis, pyelonephritis, unresolved toxæmia of pregnancy and lead poisoning, show a pronounced tendency, as the disease progresses, to lose their several identities and to pursue a common course, which is best described by the noncommital term "chronic hypertensive renal disease". The symptoms and signs of this disease are those of progressive renal failure with hypertension, and the histological counterpart is the picture which has generally been labelled "chronic interstitial nephritis". The disease unfolds steadily over a period measured in years or even in decades; but in some cases there is a progressive acceleration of the process towards the end, the patient displaying symptoms which are seen in their purest form in the malignant form of essential hypertension, and which, incidentally, are often attributed to the concomitant "uræmia".

The diseases mentioned—and the list is not exhaustive—evidently bring into action some common mechanism which progressively overshadows the original abnormality. What is this common mechanism, whence does it arise, why does it assume such a dominant role, and how has it contrived so long to avoid recognition? It is now possible to give fairly convincing answers to these questions. In the first place, it has been shown that the picture of "chronic interstitial nephritis" can be faithfully reproduced by the induction of simple hypertension in a laboratory animal. It therefore seems clear that the mechanism in question is the hypertension which is common to all diseases pursuing this common course. Secondly, it seems evident from Goldblatt's work that the hypertension which appears in the course of established renal disease is an expression of renal ischæmia. While this accounts for the mixed pedigree of renal hypertension, it does not, however, imply that essential hypertension is necessarily renal in origin. Thirdly, the dominant role of hypertension is fully explained by the conception of the vicious circle, for if hypertension is able by causing renal damage to breed further hypertension, its ascendancy over any primary renal disease is clearly only a matter of time.

The fact that the effects of hypertension have escaped recognition is attributable to several circumstances. Since renal damage and hypertension can be both cause and effect of one another, it is evident that the symptoms, signs and lesions of the two processes must be closely entangled. Furthermore, in many cases of chronic hypertensive renal disease the primary abnormality is, if not frankly inflammatory, at least related to bacterial infection, and the encroachment of hypertension is accomplished in such insensible stages that the clinician has not unnaturally attributed the later manifestations to the persistence of an inflammatory process, which may in reality have been long since spent. And hypertension has completed the deception by mimicking the picture of inflammation closely enough to mislead histologists of the first rank.

Hypertension, therefore, plays a more important part than has been realized in shaping the end of chronic Bright's disease. But in emphasizing this, it is important to avoid overstating the case. Hypertension does not always intrude in chronic renal disease, nor, when it does so, is it always successful in obliterating all trace of the primary lesion. Thus some cases of primary nephritis and many cases of pyelonephritis, especially when hypertension is not clinically conspicuous, contrive to retain their identity, partly or wholly, to the end.

In the searching of histological material for evidence of primary nephritis, useful information can generally be gleaned from the distribution of the lesions. Hypertensive lesions are characteristically focal in disposition. The process seems to consist of repeated attacks at random on isolated branches of the renal artery, and as one vessel with its dependant nephrons is left crippled, another comes under fire, until eventually little or no healthy renal tissue remains. Accordingly, it is usual to find in a single section examples of all stages of the process, a different picture presenting itself in each successive field. In primary nephritis, on the other hand, the process is typically diffuse, and the picture remains substantially unchanged from one field to the next.

A knowledge of exactly what lesions can be dismissed as hypertensive clearly simplifies the task of analysing post-mortem material. Nevertheless, in many cases the final picture is wholly hypertensive in nature, and if the clinical history gives no clue to the original source of the raised pressure, the only honest diagnosis is "chronic hypertensive renal disease".

The Classification of Bright's Disease.

The foregoing remarks point to a conclusion which should have been obvious from first principles—namely, that an acceptable classification of Bright's disease can be derived only from studies of the natural history of the disease as a whole. Notable progress in this direction has been made by Ellis[2] and his pupils, whose work suggests that although there is much to learn, the available facts about Bright's disease can already be integrated into a simple design. If we confine our attention to hypertension, it is possible to draw from Ellis's classification a fairly simple diagram of the natural history of hypertension.

A diagram of this kind is inevitably an oversimplification, for there can be no finality in the understanding of disease. In some conditions included in the "miscellaneous" group the hypertension is nothing more than a complication of primary renal disease. In others, such as basophilism, lead poisoning and toxæmia of pregnancy, hypertension may appear before any evidence of renal injury can be detected, and these conditions are therefore more closely related to essential hypertension. But toxæmia of pregnancy and lead poisoning differ in important respects from essential hypertension. The hypertension to which they give rise cannot be called benign, since it usually leads to renal failure. On the other hand, the involvement of the kidney is often so gradual that the term "malignant" is hardly appropriate. In this connexion it is interesting to note that Ellis believes that there occurs sometimes a form of true essential hypertension in which renal impairment develops gradually over a period of years, and which cannot accurately be called "malignant hypertension". A similar sequence is common in the hypertensive rat; but the clinical counterpart seems hitherto to have escaped recognition.

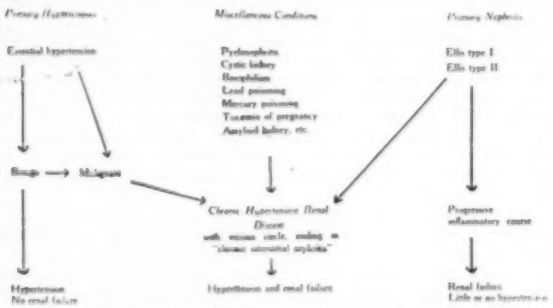

Diagram showing the natural history of hypertension (after Ellis[6]).

Lead Poisoning and "Chronic Nephritis".

The association of lead poisoning and Bright's disease is of particular interest to practitioners in Queensland, where, I understand, the incidence of infantile plumbism and of fatal "chronic nephritis" in young adults is, or has been, considerably higher than elsewhere. I am not familiar with all the evidence bearing on this question; but there is no doubt that lead poisoning commonly causes a form of chronic hypertensive renal disease, the symptoms, signs and lesions of which would, when judged by the older criteria, inevitably be attributed to inflammatory renal disease, but are, in the light of our findings, wholly attributable to hypertension.

Benign Hypertension.

It is a rather perplexing fact that, although experimental hypertension commonly though not invariably causes widespread and progressive renal damage, the great majority of patients with essential hypertension remain entirely free from renal complications. It is possible that benign hypertension arises more gradually than the malignant form and allows the arteries to protect themselves by becoming hypertrophied. This is a plausible surmise, but nothing more.

The Cause of Essential Hypertension.

I have already mentioned that Goldblatt's work has led many writers to infer that all hypertension is renal in origin, the "essential" variety being attributed to "arteriosclerosis" of the renal arteries. "Arteriosclerosis" is not a very explicit term, and my teacher, Professor Turnbull, has always discouraged its use; but I take it to refer to a structural degenerative change in the vessel wall which may impede circulation either by constricting the lumen or by preventing normal variations in muscular tone. Lesions of this kind are certainly present in hypertension, but they are more marked in long-standing cases and may be inconspicuous in the early stages of malignant hypertension. Similar lesions are also present in extreme old age in non-hypertensive subjects. In the hypertensive rat sclerotic vascular lesions are absent from the clamped kidney, but appear in the unclamped kidney in increasing degree as the hypertension persists. These facts support the view that sclerotic lesions are a result of the extra wear and tear imposed on the vessels by the raised blood pressure—a view which is held by most authorities. For this reason it is difficult to accept, without convincing evidence, the view that these lesions are the cause as well as the effect of essential hypertension.

The question is not merely of academic interest, and one point seems to have escaped attention. The arteriosclerosis hypothesis suggests, if it does not imply outright, an irreversible obstruction to the blood flow through the kidney, and we have seen that renal ischæmia of this kind certainly occurs when the vicious circle has been set in train. It is established that the immediate abnormality in hypertension is a generalized increase in peripheral arteriolar resistance, and it is widely believed that in chronic hypertension the obstruction becomes structural and therefore irreversible in nature, a belief which is reflected in the use of such terms as "arteriolosclerosis" and "arterio-capillary fibrosis".

It seems unlikely, from a consideration of the hydrodynamics of the circulation, that generalized arteriolar rigidity would be compatible with life, except perhaps at a very vegetative *tempo*. But there is more direct evidence that this belief is unfounded. It has been shown[9] that in all stages of human hypertension arterioles of the limbs will relax under the influence of warmth and other stimuli just as fully and as promptly as in the healthy subject. It is unfortunately not possible to study directly the visceral circulation; but indirect evidence suggests that there is no extensive impairment of that ability to shunt blood which is dependent on supple arterioles.

The recognition that hypertension is a response to a generalized functional hypertonus of the arterioles has prompted several groups of workers to search for an antipressor substance which will counteract the spasm of the hypertensive subject. There is direct experimental evidence that the normal kidney has considerable powers of inhibiting hypertension, and some renal extracts have distinct depressor properties. It is not yet clear that the latter effects are not merely toxic, but there is good reason to hope that an effective depressor principle will eventually be isolated. The importance of the foregoing considerations lies in the probability that if the renal vessels do not share in the response to such a principle, the renal ischæmia will merely be aggravated by the lowering of blood pressure and hypertension will be cured only at the cost of renal failure. I do not think that the facts warrant such a gloomy view of a disease which has, after all, earned the title "benign". The cause of essential hypertension clearly remains unknown, and I believe that the benign form will prove to be a functional abnormality which is reversible, at any rate in the early stages, and possibly to the end.

Hypertension and Unilateral Disease of the Kidney.

During the past few years workers in many parts of the world have been on the lookout for evidence of renal disease in patients with essential hypertension, in the hope that if the renal disease is confined to one side, removal of the diseased kidney may cure the hypertension. Many reports have now been published, and some dramatic cures have been described. But in many cases the results of nephrectomy have been less encouraging. No doubt this is partly due to the fact that neither hypertension nor unilateral renal disease is particularly uncommon, and the association must in some cases be merely fortuitous. But there is a more important reason for failure. The analogy between the patient with hypertension arising from a diseased kidney and the rat with one renal artery constricted is very close. Several cases have indeed been described in which atrophic pyelonephritis was present in one kidney and the lesions of malignant hypertension were

found in the other.[10] It has been shown that in the laboratory animal removal of the ischæmic kidney relieves the hypertension only if the operation is performed before the development of extensive hypertensive lesions in the opposite kidney. Once the vicious circle has been set in train, nephrectomy fails to abolish the hypertension, and may, moreover, aggravate matters by throwing extra work on an already damaged kidney.

These facts suggest that, although it is worth while looking for unilateral renal disease in cases of apparently "essential" hypertension, the operation of nephrectomy should not be lightly undertaken.

ACKNOWLEDGEMENTS.

In conclusion, I should like to mention that the experimental work which I have described was made possible by the generosity of Professor H. M. Turnbull in placing freely at our disposal the facilities of the Bernhard Baron Institute at the London Hospital. Several of the illustrations have already appeared in *The Lancet* and *The Quarterly Journal of Medicine*.

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ACUTE LARYNGO-TRACHEO-BRONCHITIS.

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ACUTE LARYNGO-TRACHEO-BRONCHITIS is a severe descending infection of the respiratory tract in young children, characterized by fever, toxæmia and intense inflammation of the mucosa of the larynx, trachea and bronchi. In the early stages œdema of the larynx produces respiratory obstruction severe enough to require surgical intervention for its relief; in the later stages life is threatened by a thick, viscid, crusting exudate which blocks the lumen of the trachea and bronchi.

Restriction of the term "acute laryngo-tracheo-bronchitis" to cases in which the obstructive laryngeal dyspnœa is sufficient to warrant tracheotomy is arbitrary, but it has the authority of Brighton[1] and other writers. Also, it is convenient and practical. Nobody who has seen the disease in its severe form will deny that it deserves recognition as a separate clinical entity; but the milder cases would blend insensibly with those of catarrhal laryngitis and tracheitis unless some arbitrary separation was made.

Acute laryngo-tracheo-bronchitis has been recognized in the United States of America since 1920, when Gittins[9] "realized for the first time that there were cases of serious laryngitis and tracheobronchitis in young children in which the onset and clinical picture simulated diphtheria, but in which antitoxin gave no relief and mechanical obstruction below the cannula was decidedly more troublesome than in true diphtheria". Since then there have been many reports from the United States of America to show that the disease is far from rare. Brighton,[1] for example, described a series of 27 cases from his own experience; Orton[2] reported 16 cases observed at the Essex County Hospital for Infectious Diseases during a period of fourteen months; Brennemann[4] found 45 cases in ten years at the Chicago Children's Memorial Hospital.

It is all the more remarkable that there seem to have been only three references to acute laryngo-tracheo-bronchitis in the Australian literature. Mathew[5] and Beare[6] were feeling after it in 1930 when they wrote papers on "a disease simulating laryngeal diphtheria", and Arden[7] in 1940 wrote a brief description with some case histories. This neglect is most surprising, because the condition is not really uncommon, and is at the same time one of the most harassing and alarming that a practitioner may ever have to treat.

The object of this paper is to report five recent cases and to give a full account of the disease, so that it may be recognized by Australian practitioners, for, as Kayser[8] claims, "the recognition of acute laryngotracheo-bronchitis as a clinical entity is a step in the direction of saving many young patients whose condition would otherwise be considered hopeless".

No doubt three factors have caused the disease to be so generally overlooked: (i) its tendency to occur during epidemics of catarrhal laryngitis and "influenza", (ii) its resemblance in the early stages to laryngeal diphtheria, (iii) its resemblance in the later stages to broncho-pneumonia.

Gittins[9] has "received the impression that the condition is recognised and reported in a considerable number of cases only in the localities where the otolaryngologists have been definitely interested themselves and have consequently stimulated interest and respect for the disease among the general physicians". It must be borne in mind that, in years to come, as more Australian children are immunized against diphtheria, non-diphtheritic infections of the larynx will assume ever greater importance.

It has been the general experience that odd cases of acute laryngo-tracheo-bronchitis occur at long intervals, but that small epidemics occur from time to time, sometimes in association with epidemics of "influenza" or other catarrhal disorders of the upper portion of the respiratory tract. One of us has reported that out of fifteen cases recorded in eight years at the Adelaide Children's Hospital, six occurred in one period of seven months, while at the same time the admissions to hospital due to acute catarrhal laryngitis were increased approximately eightfold.[7] During the past five years only an occasional child has been treated for acute laryngo-tracheo-bronchitis at the Hospital for Sick Children, Brisbane. However, a little girl died of the disease in April, 1943, and four other children were admitted to the hospital in June and July. These five cases will be reported in detail in this paper. It is noteworthy that this little outbreak has occurred during a season when respiratory tract infections of all kinds have been exceptionally prevalent. Gittins[9] states that he has not encountered the disease in epidemic form. His 37 cases occurred one at a time, which was in contrast to the incidence of diphtheria.

Ætiology.

In a review of the literature on the subject of ætiology,[1][9][10][11][12] the most significant fact is the variety of organisms incriminated. That a disease with such

uniform pathological effects is due to such a variety of causes is in the highest degree unlikely, and, on this score alone, we should have to look for some other cause outside the pyogenic bacteria. In the absence of any direct evidence, we have to resort to deducing the ætiology from the pathological findings. Before we go on to discuss this aspect, however, it may be well to exclude the only bacillary condition likely to be incriminated—namely, diphtheria. Clinically, diphtheria organisms were never found in any of our cases in swabs from the fauces or in the material aspirated from the trachea through the tracheotomy wound. In addition to this, the pathological appearances, macroscopically and microscopically, are quite different from those of diphtheria. Apart from any other feature, the outstanding fact in the pathology of this disease is the complete, widespread necrosis of the mucosa unaccompanied by any cellular exudate. This is not the case in diphtheria, and we shall have occasion to refer later to the microscopically obvious differences between the two diseases.

In our opinion, the evidence in favour of a virus infection seems to be overwhelming, though, of course, we have not yet been able to isolate a virus, and still less, to reproduce the disease in laboratory animals. A comparison, however, between the pathological findings in our cases and experimental laryngo-tracheitis virus infections in chick embryos[12] shows many points of close identity between the two diseases.

Pathological Findings.

In the second case in which autopsy was performed (Case III), on opening the chest, we found a complete collapse of the right lung due to complete obstruction of the main bronchus by exudate; but in both lungs in both autopsy cases lesions were strikingly absent, a few isolated, small areas of congestion being the only obvious change. With the exception of the one mentioned the other three lungs were well expanded and of good colour and had normal consistency on palpation.

When the upper parts of the respiratory tracts of the two patients who came to autopsy were opened, almost identical lesions were revealed. In the larynx sufficient swelling of the loose sub-glottic tissue had occurred to obstruct the lumen. In the trachea a striking feature was the thick, gummy exudate, which extended down to the main bronchi. In places this gummy exudate was so thick as to be crusty, and the crusts could be peeled off like a scab from a healing wound. The nature and consistency of this exudate are, in our opinion, of the highest importance, since it is the sole means by which the characteristic respiratory obstruction occurs, and the fundamental pathology of the disease is associated with this feature.

When the crusts and exudate were removed, the underlying trachea was a dirty, brownish purple colour completely lacking lustre, but quite different from the bright, purplish-red commonly found in influenzal infections. The exudate, which contained pus and was occasionally yellowish, extended down into the main bronchi, but not much farther into the lungs.

Histological investigation of the lesion gives a full explanation of these phenomena. Examination of sections reveals a complete and apparently rapid destruction of the mucosa. Not a single epithelial cell of the sections we examined was left for study. All that remained was pale, eosinophilic debris of the nature of a fibrinoid degeneration. At no place, then, within the scope of the original lesion was there any cellular exudate. There were, on the surface of the debris, a few neutrophile cells. We do not believe that these cells can be regarded in any sense as an essential feature of the lesion. They merely represent a secondary suppuration superimposed on the original necrotic lesion. Section shows that considerable vascular dilatation has occurred in the sub-mucosa, and here again, whatever cellular exudate is present is relatively scanty and entirely of a lymphocytic type.

Such a combination of phenomena is so entirely unlike those of any known bacillary infection that a bacillus as an ætiological agent can with certainty be excluded, whilst the resemblance to a typical virus infection is striking.

If we look more deeply below the vascular zone, we find a most arresting feature—namely, the complete integrity of the mucus-secreting glands. This point, incidentally, excludes diphtheria, as does the universal nature of the epithelial necrosis. The persistence of the mucous glands and their ducts combines with the secondary infection to produce the necrotic material lying on the surface of the trachea, which will necessarily be thick, gummy and purulent—so thick, indeed, as to cause respiratory obstruction and death from asphyxia.

Contrary to the usual findings in influenzal infections, the lungs are not involved in these cases, and for that reason we believe that the virus which causes this disease is not identical with the virus of influenza. This view is partially confirmed by the findings of Burnet and Foley in the paper referred to, in which they point out the difference between laryngo-tracheitis and influenza virus infections in chick embryos. Examination of sections of the lungs, in whatever areas appear to be involved, reveals infective bronchitis, but absolutely no bronchopneumonia. There is a certain amount of pulmonary œdema and no more. It would appear that death from asphyxia is so rapid that secondary bronchopneumonia has no time to occur.

From all points of view, then, we believe that we are dealing with a disease which has a specific and uniform pathology, which cannot be accounted for by any bacterial infection, but which on the contrary, in our opinion, is due to a virus. This virus, at the same time, is not an influenza virus, though we do tentatively suggest that there may be some relation between the two viruses.

Symptoms and Signs.

Acute laryngo-tracheo-bronchitis is a disease of young children. The average age in one large series was two years.[1] A case with recovery has been reported in an infant, aged only five weeks.[14]

The onset is fairly rapid, with fever, hoarseness and a croupy cough. The child may have been in good health previously, or he may have been suffering from coryza, or from one of the exanthemata. Before long noisy breathing is noticed, and within a short while hoarseness becomes more pronounced and dyspnœa develops. Ultimately the child has loud stridor, with recession of the epigastrium, the chest wall and the soft tissues at the root of the neck on inspiration. As the degree of respiratory obstruction increases, the signs of anoxæmia present themselves; the pulse rate and respiration rate rise, and the child becomes restless and terrified and throws himself about the bed, gasping for breath; the colour changes from dusky red to blue and finally to grey as circulatory failure supervenes. The progress of the disease is fairly rapid, and surgical relief is usually required within twenty-four to forty-eight hours of the onset of symptoms.

At this stage the only condition with which acute laryngo-tracheo-bronchitis is likely to be confused is laryngeal diphtheria, because the child's symptoms, and particularly the toxæmia and the degree of obstruction, are more severe than one would expect with simple catarrhal laryngitis. The distinction from diphtheria is by no means easy. Absence of membrane from the fauces is suggestive but not conclusive. The temperature tends to be higher in laryngo-tracheo-bronchitis, although it was not so in our cases. The onset of laryngeal diphtheria is likely to be more gradual, and may extend over three or four days. Finally, the child may have been immunized, in which case laryngitis severe enough to require surgical relief is unlikely to be diphtheritic.

Almost every writer advises the use of the laryngoscope for making the differential diagnosis. But if facilities for this are lacking, it is not until he performs the necessary tracheotomy that the medical attendant discovers to his dismay with what manner of disease he is dealing. Instead of opening the pale, clean, empty and apparently normal trachea of the laryngeal diphtheria subject, he finds thick mucopus, and when he has cleared this away he sees the red mucosa of an inflamed trachea.

The endoscopic appearances at this stage have been vividly described by the Jacksons:[13]

> The larynx is intensely red and the subglottic tissues on each side extend medianward, showing as mounding, red, elliptic folds, one below each cord. These swellings are peculiar to children and are due to the loose connective tissue in the conus elasticus in childhood. Small masses of secretion may be seen, but they can be wiped away cleanly, leaving no eroded or bleeding surface; there is no ulceration, no membrane. The living pathology of the bronchi is interesting and important. The mucosa is red, swollen and velvety. The rings so characteristic of the normal are obliterated. This is usually a red œdema, not the pale watery kind. The spurs between branch bronchi show distinctly the swelling of the mucosa. . . . The mucosa may be oozing blood at points. The secretions are noted as thick and tenacious, sometimes stretching in strings from one wall to the other across the lumen. Some orifices are noted as filled with pus and absence of bubbling indicates no passage of air.

For twelve hours after the tracheotomy or perhaps more, the child is quiet and comfortable, sleeping much of the time. Then his breathing becomes more laboured, rather high-pitched, almost whistling. All the bubbling noises have gone, and the trachea sounds quite dry. Retraction of the suprasternal notch reappears. The airway is closing up and the child, sensing this, becomes first restless, then panic-stricken. This stage marks the onset of obstruction in the lower part of the trachea and the bronchi. The exudate is now thick enough to cause a decided narrowing of the tracheal lumen. In some instances, to quote Brennemann,[6] it causes "such a narrowing that even the smallest aspirator cannot be passed where previously a small bronchoscope had entered".

At first it is possible to relieve the struggling child by removing some mucopus and maybe a few sticky, fibrinous crusts by aspiration of the lower part of the trachea. He returns to his cot breathing more or less freely, but not for long. Within a few hours the ominous symptoms have returned. Once again the terrified child must submit to suction through a bronchoscope or gum-elastic catheter before he can get his breath. For the next three days or so, perhaps at intervals of a few hours, the ghastly procedure may have to be repeated.

It is not surprising that only half of these children recover. The condition of those who do usually improves about three or four days after the performance of tracheotomy. The temperature settles down, and the intervals between suctions grow longer. Best of all, the dry, whistling breathing disappears, and the air passing in and out of the tracheotomy tube makes a fine bubbling sound. The tracheal and bronchial secretions become wet and loose and can be coughed up. At the same time the laryngeal swelling subsides, and the tracheotomy tube can be taken out about the seventh day. Thereafter recovery is usually uninterrupted, though slow. Bronchopneumonia occurs less commonly than one might expect, particularly if the child has been taking sulphathiazole from the start.

Many other children cannot stand the enormous strain which this illness involves. They may die in the early stages from toxæmia and laryngeal obstruction, or become worn out by the repeated spells of partial anoxæmia followed by the pain and shock of tracheal suction or bronchoscopy. But they die most frequently because the thick, purulent exudate does not confine itself to the trachea, but extends into the bronchi and even into their finer branches. When this happens, portions of the lungs collapse and the breath sounds disappear. The thoracic cage moves rapidly up and down, but little air can be heard passing to and fro in the tracheotomy tube. If too much lung tissue is shut off, the child's colour changes; but there is remarkably little struggling, and very often he falls asleep before he dies.

Treatment.

The treatment of acute laryngo-tracheo-bronchitis must perforce begin before the diagnosis is settled, for at first the child simply has "croup". At this stage a steam tent is needed, and some such sedative as chloral or phenobarbital to relieve laryngeal spasm. Since the respiratory tract is inflamed, sulphapyridine is indicated, and as one cannot be sure—even in the absence of membrane from the fauces—that the case is not one of laryngeal diphtheria, and as the neglect of laryngeal diphtheria is so deadly, a substantial dose of antitoxin (20,000 units) should be given at once. Finally, the nurse should observe her patient carefully for signs of increasing obstruction of his airway, recording the pulse and respiration rates every quarter of an hour. On no account should morphine be given to control restlessness, as it would mask the symptoms of anoxæmia.

It is always hard to decide whether the time for surgical intervention has come. Nobody can lightly subject a child to tracheotomy unless he considers it essential; yet it is neither wise nor kind to allow him to struggle on for hours, tiring himself out, when every inspiration is an effort and the pulse rate is rising. On the whole there is a tendency to wait too long, because of the pernicious teaching that pallor, sweating, cyanosis and extreme restlessness are the indications for operation. Actually they are the symptoms of anoxæmia, and indicate impending death or permanent damage to the cells of the brain.

Tracheotomy performed reasonably early can be done carefully, with a minimum of shock, and it leaves the child in better condition to contend with the hazards still ahead. Local anæsthesia is used. Infiltration of the tissues makes them partly translucent, and after the skin incision the whole operation is carried out by blunt dissection until the trachea is exposed. Veins are gently drawn aside instead of being divided, and there is practically no bleeding. The opening in the trachea should always be below the isthmus of the thyreoid; the sensitive cricoid region is thus avoided.

The violent coughing spasms which occur as soon as the tracheal dilators are opened are advantageous, for they help to expel the mucopus which, even at this stage, is beginning to collect in the trachea. Before the tracheotomy tube is inserted, it is wise to carry out gentle aspiration with a well-lubricated rubber catheter attached to a suction pump. Material for cultural examination should be taken from the lumen of the trachea to ascertain the predominant organism, as this may affect the subsequent chemotherapy. If, for example, *Staphylococcus aureus* was found in pure culture, sulphathiazole or sulphadiazine would be more suitable for the child than sulphapyridine. One should insert and tie in position as large a tracheotomy tube as possible; an infant of twelve months can always take a number 18 tube, and a child of four years a number 22 tube.

The grim battle to keep the child's airway clear during the next few days demands the most skilled nursing and constant attention. The principal danger is that the tracheo-bronchial secretions will become dry, sticky and crusted. To combat this, the atmosphere around the cot must be saturated with moisture from steam kettles or humidifiers. Orton,[5] McCaskey[10] and others have pointed out that children do far better in a thoroughly humidified room, kept at about 70° F., than in the old-fashioned, hot steam tent. A cold humidifying apparatus will fulfill these conditions. In addition, the child himself must be made almost sodden with fluid. If he cannot be persuaded to drink much, he must be given water by the rectum or by nasal tube, or, if necessary, intravenously.

Direct methods of keeping the air passages moist must be employed also. A warm, sterile 5% solution of sodium bicarbonate in distilled water helps to soften and dissolve the gummy secretions in the trachea, and a few drops of this solution may safely be dropped into the opening of the tracheotomy tube every half hour. An immediate coughing bout follows, and the child generally expels some mucopurulent material, the removal of which can be assisted by suction through a rubber catheter momentarily inserted through the tracheotomy tube. A skilled nurse can manage this manœuvre successfully without medical aid.

Galloway[17] and Neffson[12] advocate limited lavage of the trachea. They instil five to fifteen cubic centimetres of 5% sodium bicarbonate solution, and then carry out immediate aspiration with the patient's head low.

Galloway, in fact, attaches much importance to postural drainage in the treatment of this disease, pointing out that the tracheo-bronchial secretions are fluid when first formed, and that the nearer to the outlet they can be persuaded to flow before drying up, the easier will their subsequent removal be.

However, it is seldom that such simple measures suffice for more than twelve to twenty-four hours after the performance of tracheotomy. A time usually comes when the signs of respiratory obstruction return, and the nurse reports that she can no longer pass a soft rubber catheter along the trachea. More drastic treatment is now required, or the child will soon die. The best manœuvre, if expert assistance is at hand, is for a bronchoscope to be passed through the tracheotomy incision, so that the sticky crusts and plugs may be picked off the wall of the trachea and from the orifices of the bronchi with forceps. Fluid secretions dammed back below the plugs may then be aspirated.

There is no time to waste, however, and if no skilled bronchoscopist is at hand, the next best procedure is to put the child on the operating table under a good light, remove the tracheotomy tube, open the trachea with dilators and pass down it a gum-elastic cathether attached to a powerful suction apparatus. The catheter should be well lubricated with cotton-seed oil; it should be of about number 8 gauge, and the end should be cut off. The instillation of a few drops of sodium bicarbonate solution should precede each passage of the catheter. This procedure may have to be repeated several times in quick succession before the airway is free. So nearly obliterated may the lumen of the trachea be by the fibrinous exudate that some force may be required to pass the catheter at all. It is an agonizing experience, and stimulants are required for the child. When he can once again breathe freely, the tracheotomy tube is reinserted.

Within a few hours the whole procedure may have to be undertaken again. LeJeune and Bayon[3] reported a case in which bronchoscopic aspiration had to be repeated on 29 occasions over a period of several days.

About the only consolation that can be offered to the parents during this harrowing time is that, if their child can be kept alive for about four days, spontaneous recovery will set in. The nurse must be constantly on the watch for the recurring attacks of tracheal obstruction, which may come on with surprising suddenness. Hospitals treating these patients need an alarm bell system capable of summoning medical aid on the instant, at any hour of the day or night. The child himself should be disturbed as little as possible, except for drinks. A stimulant is needed from time to time, especially after aspiration of the trachea. Perhaps the most suitable is a few minims of neat brandy, given on a teaspoon. Oxygen is of some value, especially in those cases in which even the most complete suction does not entirely free the airway, and portions of the lung remain collapsed. These are the unfavourable cases in which the viscid secretion is causing obstruction in the smaller bronchi. Once this happens, and the physician finds that the obstructing material is beyond the reach of his smallest aspirator, there is little more to be done. He can only stand unhappily by, waiting for the end.

In favourable cases the secretions become looser about the fourth day after tracheotomy, and the most dangerous period has passed. When the laryngeal œdema subsides, the orifice of the tracheotomy tube can be gradually closed. If this causes no distress, the tube can be removed, usually about the seventh day. Chemotherapy should be continued until the temperature has been normal for two days. Rest in bed is necessary for another fortnight.

Comment.

From the foregoing description it will be obvious that the prognosis is always serious. According to the Jacksons,[2] recovery occurs in not more than 50% of cases under the best possible conditions. Gittins[5] had 37 patients requiring tracheotomy, with a mortality rate of 51·3%. Other writers who claim lower death rates have included milder cases, in which recovery followed medical treatment alone. This is misleading, because, as we have shown, there is no clear-cut separation between the milder forms of this disease and the catarrhal type of laryngo-tracheitis.

Nevertheless, some of the most recent writers hold that the outlook can be improved. Orton,[1] in 1941, reported sixteen cases in which tracheotomy was required, with a mortality rate of only 31%, and Kayser,[4] in a review of recent literature, concluded that by cooperation between physician and laryngologist and with "unremitting and meticulous vigilance by trained assistants", the mortality rate could be reduced to 25% or even less.

It is not so many years since physicians, if they recognized the disease at all, despaired of treating it. Four factors have contributed to the improved outlook at the present day. These are: (i) recognition of acute laryngo-tracheo-bronchitis as a clinical entity; (ii) early relief of laryngeal obstruction by tracheotomy; (iii) insistence that the air breathed by the child after tracheotomy should be saturated with water vapour; (iv) the use of the bronchoscope to overcome bronchial obstruction. It is our hope that the disease will be more widely recognized by Australian practitioners in the future, so that the appropriate treatment may be undertaken.

Reports of Cases.

The following reports describe five recent cases from the Hospital for Sick Children, Brisbane.

CASE I.—D.J., a girl, aged four years, was admitted to hospital on April 6, 1943. She had complained of a sore throat on going to bed, and woke at 3 a.m. having difficulty with her breathing. Her condition became rapidly worse, inspiration being loud and crowing and her colour dusky. A doctor was called at 6 a.m., and the child arrived at the hospital at 8 a.m. after a fifty-mile ambulance journey. She was then scarcely able to breathe and was unconscious, deeply cyanotic about the lips and pale elsewhere. Immediate tracheotomy was performed, but respiration ceased entirely and for some minutes she appeared almost dead. Breathing finally recommenced after prolonged artificial respiration and the administration of "Carbogen" and stimulants. However, although her airway was now clear, the child did not fully regain consciousness. Her temperature rose rapidly to 104° F., she had repeated convulsions during the day, and died eighteen hours after her admission to hospital.

At autopsy the larynx was acutely inflamed and so œdematous as to be completely obstructed. The mucosa of the whole respiratory tract, from the pharynx to the smallest bronchi, was intensely red. The lungs were a little congested. No diphtheria membrane was present. Incubation of material taken from the larynx produced only *Staphylococcus aureus*.

CASE II.—P.C., a boy, aged four years, was admitted to hospital on June 27, 1943, at 10 a.m. He had been "off colour" for the past week and had suffered from "difficult breathing" for the previous three nights. His temperature on admission to hospital was 99·2° F. and his pulse rate 120 per minute. He looked ill and had some stridor and dyspnœa and a croupy cough, with slight recession of the epigastrium and suprasternal notch; but his colour was good and he was not restless. His throat was inflamed, but free from membrane. Examination of the chest revealed nothing beyond transmitted laryngeal stridor.

Not being ill enough for tracheotomy, he was treated with a sedative and put in a steam tent, and was given 30,000 units of diphtheria antitoxin; he was also given an initial dose of one gramme of sulphapyridine, followed by 0·5 gramme every four hours. For a while he remained fairly comfortable; but next day (June 28) the laryngeal obstruction increased abruptly, and tracheotomy was performed about 4 p.m.

During that night and the following day he was fairly comfortable and breathed quite freely through his tracheotomy tube. By the evening of June 29, however, he was again suffering from obstruction of his airway below the tracheotomy tube. After the removal of some mucopus and fibrinous debris from the lower part of the trachea by suction with a gum-elastic catheter he breathed freely once more, but within a few hours he was distressed again, and the procedure had to be repeated. The next seventy-two hours must have been a ghastly nightmare to the child. He will remember struggling for breath almost to the point of asphyxia; the pain of having a stiff catheter forced down

an inflamed trachea; the relapse into unconsciousness from anoxæmia and shock; the few hours of exhausted sleep before the dreaded tightness of his breathing returned. During this period his trachea was aspirated on fifteen occasions. The temperature remained fairly steady between 99° and 100° F. The pulse rate was 140 to 160 per minute. No diphtheria bacilli were found in repeated swabbings from his throat and trachea, from which *Staphylococcus aureus* was grown in pure culture. Sulphathiazole in the same dosage was substituted for sulphapyridine on June 29.

Improvement in his condition began on the evening of July 2, with the extraction of several fibrinous plugs from the trachea. The largest one was about the size and shape of a date-stone, made of compressed fibrin and quite hard. Next day he was much better. The tracheal secretions were looser, instead of being gummy and viscid, and could be coughed up. The laryngeal obstruction was also subsiding, and he was able to breathe without his tracheotomy tube. Sulphathiazole therapy was stopped on July 4, when his temperature had been normal for two days. He was very weak and exhausted, but already looked better. Scattered râles could be heard over various parts of his lungs, but he had a good air entry everywhere and no consolidation. Twice during the next ten days he had a raised temperature with a cough and indefinite chest signs, but on each occasion he responded quickly to sulphathiazole. The tracheotomy wound healed rapidly, and the boy was discharged from hospital in normal health on July 27.

CASE III.—R.S., a boy, aged fifteen months, was admitted to hospital on July 8, 1943, at 10.30 a.m. He had suffered from gradually increasing difficulty with his breathing for the previous forty-eight hours. His temperature was normal and his pulse rate was 120 per minute. He was in some respiratory distress, with inspiratory and expiratory stridor and chest recession. His colour was good. No membrane was visible in his throat. He was given 40,000 units of diphtheria antitoxin and a sedative and treated in a steam tent.

Within two hours his airway was gravely obstructed and cyanosis was commencing. Tracheotomy was performed, and a quantity of thick mucopus was found in the trachea, but no diphtheritic membrane. After suction of the trachea and the introduction of a tracheotomy tube, he was returned to his steam tent and given 0·5 gramme of sulphathiazole as an initial dose, followed by 0·25 gramme every four hours; he was also given an ipecacuanha mixture.

The child produced a quantity of thick mucopus, which kept blocking the tracheotomy tube, necessitating its frequent removal and cleaning and suction by means of a fine rubber catheter. By 3 a.m. on July 9 the secretions were so hard and viscid that the soft rubber catheter proved inadequate, and asphyxia was threatened. A gum-elastic catheter was used, and some tenacious mucopus was withdrawn from the lower part of the trachea. Afterwards the airway was better, although the child was in a state of collapse. He was revived with oxygen, brandy and "Cycliton", and returned to his steam tent. The temperature was 101° F. and his general condition was poor. Further suction of the lower portion of the trachea was required at intervals, and his condition steadily deteriorated from the intermittent anoxæmia and prolonged struggling. Death occurred next day after an obstructive attack.

Culture of material taken from the trachea when tracheotomy was performed yielded a pure culture of meningococci. Incubation of a second specimen taken on the following day produced a mixed growth of *Staphylococcus aureus*, pneumococci and meningococci. No diphtheria bacilli were found in either of these cultures or on throat swabs taken on July 8 and 9.

At autopsy, the whole of the respiratory tract was full of thick pus. No membrane was visible. The right lung was completely collapsed as a result of bronchial obstruction by thick, tenacious pus. Other organs were normal. Culture of material taken from the lung *post mortem* grew *Staphylococcus aureus* and meningococci. No diphtheria bacilli were found.

CASE IV.—L.R., a girl, aged eleven months, was admitted to hospital on July 13, 1943, at 2 p.m. She had been ill since the previous day with fever, noisy breathing and gradually increasing respiratory embarrassment. She was a well-nourished baby with a temperature of 101·6° F., and was obviously in trouble with her breathing. No membrane was visible in the throat. She was given 20,000 units of diphtheria antitoxin and a sedative, and treated in a steam tent.

For a while she was fairly comfortable, but after some hours it was evident that the respiratory obstruction was increasing. Tracheotomy was required at 11 p.m. Some mucopus but no diphtheria membrane was found in the trachea, and it was noted that although it helped her considerably, the operation did not completely relieve her respiratory obstruction. Sulphapyridine was administered from the time of the operation in doses of 0·25 gramme every four hours, but in spite of this her temperature continued to rise, and by the following afternoon it was 103·6° F. By this time throat swabs had been examined and a negative report returned, and material taken from the trachea at operation had yielded on culture no diphtheria bacilli, but numerous colonies of *Staphylococcus aureus* and a few pneumococci. Sulphathiazole was accordingly substituted for sulphapyridine on July 14.

Meanwhile her tube was repeatedly becoming blocked with thick mucopus from the trachea. By 6 a.m. on July 14 suction with a soft rubber catheter no longer sufficed, and it was necessary to remove the tube and insert a gum-elastic catheter into the trachea, to remove the viscid material that was occluding the airway. This procedure had to be repeated many times. The struggling cyanosed child would be partially relieved for a few hours, and then the same terrifying symptoms would recur. Suction as far as the bifurcation of the trachea did not completely relieve the obstruction, and she remained in a state of partial anoxæmia throughout. Although her temperature was controlled to some extent by the sulphathiazole, the pulse rate mounted steadily. Death occurred seventy-two hours after the tracheotomy, from anoxæmia and cardiac failure.

At autopsy the laryngeal mucosa was very swollen. The whole respiratory tract, from the larynx downwards, was full of very thick, pale yellow pus, which bubbled out of the main bronchi with pressure on the lungs. Patchy congestion of both lungs was present, and when they were cut, areas corresponding to the larger bronchioles were full of pus. The other organs were normal. Material from the trachea yielded a growth of *Staphylococcus aureus* in pure culture. Examination of sections of the trachea revealed necrosis of the mucosa and intense congestion of the submucosa.

CASE V.—E.T., a girl, aged six years, was admitted to hospital on July 23, 1943, at 4 p.m. She was suffering from measles, the rash having appeared three days earlier. Respiratory difficulty had commenced about eighteen hours before she came to hospital, and was then extreme; she was blue and had loud stridor and a great deal of chest recession. Immediate tracheotomy was performed, and a quantity of mucopus was found in the trachea. When this had been aspirated she felt much easier. No membrane was seen. She was returned to a steam tent and given 20,000 units of diphtheria antitoxin and one gramme of sulphathiazole followed by 0·5 gramme every four hours. Pneumococci were grown in pure culture from material taken from the trachea at the time of operation. No diphtheria bacilli were found in repeated swabbings of throat and trachea.

She was fairly comfortable for the next two days, and it was possible for a nurse using a soft rubber catheter to keep the airway clear; but on July 26 the lower part of her trachea became badly blocked on three occasions, and she could be relieved only with difficulty. Next day the secretions were looser, and she was much more comfortable. Her temperature had remained between 99° and 100° F. and her pulse rate between 110 and 130 a minute.

The laryngeal obstruction subsided enough to permit removal of the tracheotomy tube on July 28. Thereafter she recovered satisfactorily, and was discharged from hospital on August 8.

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SOME OBSERVATIONS UPON CHRONIC INFECTIVE ARTHRITIS AND AN EXPERIMENT.

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THE average general practitioner so frequently sees patients suffering from infective arthritis, and so often, as the family doctor, has the unique opportunity of following up his patients over a long period, that he gradually develops a definite and decided viewpoint in regard to this disease. Confronted with a sallow-complexioned woman of hopeful eye and weary voice, apprehensive of movement in her shining, swollen digital joints, the doctor gives a sigh of resignation and sets out upon the hunt for septic foci. At the end of some months the patient is *sans* teeth, *sans* tonsils (including always the lower poles, please), *sans* appendix and even *sans* gall-bladder at times. The duodenal tube is passed and a streptococcus is isolated or not isolated from the gastric "hide-outs". If the hunt is successful, vaccine therapy is instituted. Time passes and the hunt is renewed. The maxillary antra are radiologically examined, and—disbelieving Thomas that the general practitioner oft-times is—the same sinuses are proof-punctured, and thus assurance is rendered doubly sure. Sometimes results are happy; sometimes the patient remains the sallow-complexioned woman that she was when first she wandered into the surgery—a little the worse for wear, perhaps, but still with a tiny flame of hope and confidence burning.

The practitioner, like the lad who through the alpine village passed, never despairs, but now turns to that empirical wonder, gold therapy. All septic foci having been thoroughly eradicated, the results this time may be quite encouraging. However, time goes on, and in most cases so does the disease. The small flame still burns, and the now despairing practitioner casts about for some magic potion that will of a sudden rid the crippled body of its plague.

The following portion of this paper is the result of my having on a number of occasions reached this last stage of "checkmate" after "doing the rounds" of classical orthodox treatment.

Definition.

For the present purposes, chronic arthritis has been separated into two large categories, as suggested by Professor William Boyd.[3] These are (*a*) chronic infective arthritis and (*b*) chronic degenerative arthritis. To quote from Boyd, the points of distinction are the following:

	Infective Arthritis.	*Degenerative Arthritis.*
Sex:	Common in the female.	Common in the male.
Age:	Generally under forty.	Generally over forty.
Onset:	Gradual, but sometimes acute.	Always gradual.
Joints:	An inflammatory condition of synovial membrane. Early lesions in metacarpo-phalangeal joints and wrists; symmetrical and migratory.	A degenerative condition of cartilage and bone. Early lesions in terminal inter-phalangeal joints, hips and knees; often unilateral and fixed.
Local Signs:	Local signs of inflammation, marked deformity, extreme atrophy of muscles, swelling of soft parts, subcutaneous nodules, fibrous or bony ankylosis. Marked pain. Complete crippling of 10%.	No local inflammation. Deformity not marked; atrophy only from disuse. Soft parts not swollen. Heberden's nodes and no true ankylosis. Little or no pain. Complete crippling rare.

To this should be added the pertinent fact that in cases of infective arthritis it is usual to discover that the glands draining the affected joints are enlarged.

A Hypothetical Ætiology.

Douthwaite[3] has succinctly summed up as follows the present position in regard to rheumatoid arthritis:

> As a non-fatal disease of extreme chronicity rheumatoid arthritis provides vast scope for the most detailed investigations. In spite of the amount of work done, the results are remarkably unproductive of therapeutic aid. The only real advance which has been made in the last decade is the introduction of gold treatment, yet this arose as an empirical measure in no way related to planned research.

One need make no apology for formulating a working hypothesis concerning the ætiology of this disease. Right or wrong as it may be, a new one is here set out. Following upon an infection of tonsils, teeth or other areas, the joints become the metastatic seat of a chronic, smouldering, subacute inflammation. This inflammation is caused by the actual presence in the joints themselves, and in the glands draining those joints be it noted, of the infecting organism. Cecil[3] and Cadham[4] have isolated organisms from both the glands and the joints. The original septic foci may or may not be removed. Whether or no, from the new garrisons in the intricacies of the synoviæ and lymphatic glands the organisms continue their local maraudings and their generalized toxæmic depredations. In short, the joints and glands themselves become septic foci.

Cadham[4] has pointed out that of 500 patients who came under his care, "over 50% gave a history of removal or treatment of some suspected foci of infection without subsequently experiencing relief". The foregoing theory of the pathology would explain why. The circumstances suggesting the present investigation followed upon the rather hopeless outlook in the first case quoted below, that of Miss M.W., correlated with the ætiological propositions described.

Miss M.W. had had every available treatment in her time to ameliorate her condition, but it gradually became worse until she was reduced to crutches and even then could progress only with the assistance of someone to steady her and preserve her balance. Every movement was painful. At this juncture another patient developed acute fulminating arthritis of the knee joint following a trivial ax-cut some two and a half inches below the knee. It was argued then that if, as was probable, the infecting organism had been carried to the knee joint by the lymphatics, perhaps sulphonamide might also be carried there by the same route, and at the same time be carried on to the whole lymphatic system of glands in the lymph-way to the common lymph duct. It was determined to try the effect of "blitzing" the lymphatic system in the case of

Miss M.W. The diffusible liquid sulphonamides such as "Soluseptasine" *et cetera* were not considered, as it was possible, and indeed probable, that they would be absorbed to a great extent into the blood stream via the local capillaries. It was decided to use sulphonamide powder, which must be carried by the lymphatics almost *in toto*. The method employed and the results obtained are described with the case reports. It should perhaps be added that previously an attempt had been made by various devices to insinuate the powder directly into the joints of laboratory sheep afflicted with a common rheumatoid-like joint condition that prevails among those animals. The attempts were, for a number of reasons, unsuccessful. It was then that the unfortunate accident to the patient whose knee was infected through a small ax-cut inspired the method of inserting subcutaneous deposits of sulphonamide powder distal to the joints.

Reports of Cases.

CASE I.—Miss M.W., aged eighteen years, first consulted me in July, 1940. She was on crutches, and even so she could progress at all only with the aid of an assistant. She had a typical rheumatoid condition of practically all her joints. Her general condition was one of emaciation and her colour was sallow. She had been investigated thoroughly and treated at numerous large city hospitals and by many physicians. It is not proposed here to detail all the results of the investigations, save to recount that X-ray examinations at various times revealed no bony lesions in the joints, that the cranial sinuses were clear, and that there was no evidence of apical sepsis in the teeth. The Mantoux test and the Wassermann test produced no reaction. A blood count revealed some anæmia and leucocytosis (15,000 leucocytes per cubic millimetre). The stomach contents were sterile. A fractional test meal examination gave normal results. The urine was sterile. Her tonsils had been removed very thoroughly and appendicectomy had been performed.

Her illness had begun in 1935, with swelling in one knee, and she was recumbent for two months. The swelling later spread to other joints, and eventually she became a complete invalid. When she was first examined by me in 1940 the pain and swelling were mainly in the knee joints; the other joints, though all affected, were at the moment not giving her the same trouble. It was thought that if she could regain the use of her knees she would at least become a little more independent of assistance. To this end treatment of all types was tried for approximately twelve months, but no good results were obtained. Courses of sulphonamide by mouth were unavailing. The stage of "checkmate" had been reached.

The idea of inserting sulphonamide into the joints was toyed with and even experimented with upon affected sheep, as has been mentioned. Then it was that there occurred the trivial ax-cut in another patient, with its dramatic lymphatic spread of infection to the joint. Miss M.W. was willing to try the effect of sulphonamide deposits. For this purpose "Evipan" was administered. An incision was made, about one and a half inches long, well below the knee on the outer aspect of the leg. The subcutaneous fat was lifted from the subjacent muscles so that a "pocket" was made. Two drachms of sulphanilamide powder (sterilized) were inserted into the pocket. After four days the dressing was removed and the knee was uncovered. The knee joint was down to practically normal proportions for the first time the patient could remember. After this the other leg was dealt with in the same way, and the same result followed. With the determination to "blitz" the lymphatic system thoroughly, another incision was made a week later over the outer aspect of both thighs. This was done in June, 1941. Miss M.W.'s condition improved remarkably. She gained in weight, walked about by herself without crutches, and when last seen by me in May, 1942, she was "riding" a bicycle frame, with the idea of keeping the fullest flexion and extension of her knee joints.

CASE II.—Mrs. G.S., aged thirty-two years, was first examined by me in November, 1940. She complained of "rheumatism" in the shoulders, wrists and knees. She had had it coming on since 1938 at least. She said that when she suffered from a sore throat the pain was very severe, and at times she could not move the wrists for pain and swelling.

She was a rather fat woman with a very sallow complexion. She had early "rheumatoid" finger joints, and pain and tenderness were widespread in other joints. Her tonsils had been "guillotined" when she was at school. Her appendix had been removed. Examination, however, revealed both tonsils to be buried; thin pus exuded from the crypts, and the pillars of the tonsils had the typical "streptococcal blush".

I dissected her tonsils out carefully in December, 1940. Some slight temporary improvement followed. The ensuing years of 1941 and 1942 were occupied by the usual round of arthritic therapeusis as far as I was concerned, and with pregnancy and the advent of twins as far as the patient was concerned. Neither event improved the patient's condition. By April, 1943, the generalized arthritis had reached severely painful and crippling dimensions, and once again the stage of "checkmate" had been reached. The proposal to use sulphonamide deposits was made and accepted.

On May 8, 1943, under anæsthesia, two drachms of sulphanilamide powder were inserted into each leg by the usual pocket. The incisions were made on the outer aspects of the shins. When the patient was again examined on May 18 she had had practically no "rheumatism", but both legs were swollen, obviously from lymphatic obstruction in the sulphonamide-choked glands. This swelling gradually disappeared without the need for recumbency. When she was last examined on August 24, the patient was a fat, healthy-looking woman, of good colour and with abounding energy; she had been absolutely free from rheumatism since the date of the sulphonamide deposits. Such freedom and health she had not known for years.

Before I proceed to the next case report, a quotation, again from Boyd,[1] may here be permitted:

> The process (infective arthritis) at the commencement is essentially a synovial one, and it may never pass beyond that stage. Thus the disease might be called synovio-arthritis.

It is obviously while the disease is still in the early "synovial stage" and before the various degrees of ankylosis develop that one can expect tissue repair from any form of treatment. Despite this, however, it was decided to try the treatment with an "old, chronic rheumatoid" patient. The following case is typical.

CASE III.—Mrs. E.W.F., aged sixty years, was first examined in May, 1943. She was suffering from advanced arthritis of long standing, with gnarled, painful joints. Various forms of treatment were tried in an attempt to eradicate the actively inflammatory aspect of her joints. In addition to the usual agents, œstrogenic therapy was tried, but without avail. On June 15, 1943, subcutaneous deposits of sulphanilamide were made into the legs, and on June 22 into the forearms. The results were in no wise startling. During the next six weeks the joints became obviously less painful on movement, and the patient gained increased suppleness and new movement in her joints. It is not to be expected, however, that the destruction of years can be righted miraculously.

Comment.

The experiences gained and the results of treatment obtained in the cases reported, and from the few others omitted, are, of course, far from being of statistical value. They do, however, show what interesting avenues remain still to be explored in such a widespread, crippling condition, that might well make the persecuted victim of his pains and aches exclaim in the words of Shakespeare:

> Tired with all these, for restful death I cry!

In the majority of diseases the physiology of the affected organ or organs has been investigated at infinite length. It is a strange thing, however, that when one comes to the subject of infective arthritis, one is struck with the paucity of information obtainable in regard to the physiology of joints. So much has been written of rheumatoid arthritis and so little is known of the joints and their physiology! A strange anomaly indeed, that has been deplored by Boyd.[1] Their chemical-absorptive powers are apparently a closed book. One would like to inquire the percentage concentration of sulphonamide in the synovial fluid as compared with that in the circulating blood after oral or intramuscular therapy. It is possible that the percentage in normal synovial fluid is very small. It would be of interest to know what percentage of sulphonamide is obtainable from any lymph gland after intravenous therapy. These are but some of the questions that spring to the mind. The realms of experiment are truly vast.

It may well be held that the method of subcutaneous deposits, being irreversible, exposes the patient to the rare

chance of developing agranulocytosis. Hence, only as a last resort has this chance been taken, and in all cases the slight risk has been explained to the patient.

Finally, the method detailed above is not by any manner of means claimed to be anything save an added weapon in our armament against a most devastating disease. It is published for this reason, and with the added hope of stimulating further research by those who have more concentrated contact with the disease.

Summary.

1. Some comments from the viewpoint of the general practitioner are made in connexion with chronic infective arthritis.

2. The suggestion is made that the affected joints and glands in infective arthritis become metastatic septic foci, even though the original infecting focus has been removed.

3. A method of treating these foci by subcutaneous deposits of sulphonamide powder is promulgated with illustrative reports of cases of varying severity.

Acknowledgements.

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Reports of Cases.

A CASE OF ENCEPHALO-MYELITIS FOLLOWING VACCINATION.

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IN view of the world-wide distribution of post-vaccinal encephalo-myelitis (van Rooyen and Rhodes[1]), it seems probable that cases of the disease have occurred in Australia. The only one recorded, however, is that by Lockwood.[2] His diagnosis was based entirely on clinical evidence; no autopsy was performed. In the case now reported the diagnosis has been confirmed by pathological examination. This is believed to be the only case among approximately 50,000 persons vaccinated in South Australia during the last three years.

The relevant literature has been summarized by van Rooyen and Rhodes and by Thompson.[2]

CLINICAL RECORD.

A.B.S., aged forty-seven years, a soldier, was admitted to the Repatriation General Hospital, Keswick, on May 15, 1942. For seven days he had suffered from a sore throat, an irritating cough, mild pain in his limbs, and headache. His symptoms had been much worse for the twenty-four hours preceding his admission to hospital. The patient had been revaccinated against smallpox on April 22, 1942. (Primary vaccination was in 1916.) At the time of revaccination he had also been inoculated with "T.A.B." vaccine and tetanus toxoid. Inoculation with "T.A.B." vaccine had been repeated on May 11.

About a month before his admission to hospital, the man fell and bruised the lower lumbar portion of his spine. In December, 1941, he had suffered from abdominal colic for about a week. Examination of the dust in the quarters in which he was then living revealed 42% of lead. His blood picture, however, was not typical of lead poisoning. In 1918 he had had malaria.

Further information obtained about three months after the patient's death revealed that there had been no cases of similar illness among other soldiers. The actual number of men vaccinated with the particular batch of lymph was unknown. The patient had been vaccinated by only one insertion; inspection some days later had disclosed only a mildly red areola.

On his admission to hospital, the patient's temperature was 98·8° F. His conjunctivæ, fauces and pharynx were congested. Examination of his cardio-vascular, respiratory and digestive systems revealed no abnormality. The urine was acid in reaction and had a specific gravity of 1·030; neither albumin nor sugar was detected in it.

On the following day (May 16) his temperature had risen to 99·8° F. He complained of numbness in his left leg and in the lower part of his abdomen, and of inability to pass urine. The knee jerks were absent; the plantar reflexes were flexor in type. No definite impairment of sensation was detectable in his left leg.

Next day there was definite loss of sensation in both legs and indefinite loss in the thighs. His temperature was 102·4° F.

On May 18, his temperature had dropped slightly, to 102° F. Sensation was impaired to a level of about half-way up the abdomen. Some sensation still remained in the soles of his feet. There was some spasticity of his arms. The patient had complained of blurring of vision, but no pathological change was found in his optic fundi. The urine had an acid reaction and a specific gravity of 1·030. It contained a small quantity of albumin, but no sugar. Red blood corpuscles and bile pigment and salts were absent. The cerebro-spinal fluid was slightly opalescent and contained a small "spider-web" clot. Of the 200 white cells present per cubic millimetre, almost all were lymphocytes. There was no excess of globulin or albumin in the fluid.

On the following day his temperature was 103° F., his pulse rate was 100 per minute and his respiration rate was 30 per minute. Sensation was impaired up to the nipple line, and breathing was somewhat embarrassed. In view of the difficulty in respiration an "iron lung" was obtained; but as improvement in the man's condition occurred it was not used. A catheter was tied in, and bladder wash-outs were given daily. The diagnosis made at this stage was "toxic polyneuritis, possibly influenzal in origin".

On May 22 the patient's temperature was 100° F. The skin over the sacrum was somewhat reddened; later it became necrotic. He had an irritating cough associated with some moist râles at the bases of his lungs.

On May 24 respiration was less embarrassed. The level of impairment of sensation had fallen from the nipple line to the umbilicus. His vision was unaffected. The knee and ankle jerks were absent.

Two days later the level of sensory loss had fallen to a line midway between the umbilicus and the *symphysis pubis*. The patient was able to move his great toes.

On May 29 his temperature was 102° F. The degree of movement possible in his feet had increased. The knee and ankle jerks were absent. There was a large, sloughing, ulcerated area overlying the sacrum and lower lumbar region.

On June 3 the patient's temperature was 101° F., and his respirations numbered 24 per minute. From then on there was no appreciable change in his condition until June 18. The level of sensory loss remained at about the umbilicus. The extensive bed sore in the lumbo-sacral region was associated with a "swinging" temperature. The man's condition was much worse on June 18; his temperature was 103° F. and his pulse rate was 108 per minute.

On June 26 the level of sensory impairment was at the pelvic spines. He was unable to move his toes. Moist râles were detectable at the bases of both lungs. His temperature was 102° F., his pulse rate was 110 per minute, and his respirations numbered 30 per minute. The patient died on July 2, 1942.

POST-MORTEM EXAMINATION.

Autopsy was performed on July 3, about nineteen hours after the patient's death. The brain was soft, probably from post-mortem degeneration. In the lumbo-sacral region there was a large bed sore with a sloughing base, in which the underlying bone was revealed; the ulcer measured about

[1] Work done with a grant from the National Health and Medical Research Council.

five inches by five inches. The bases of the lungs were congested. No pleuritic adhesions were present. The spleen was large and soft. The liver was also enlarged, and cloudy swelling was apparent in it. Numerous miliary abscesses were present in the right kidney, the cut surface of which was pale; pus was also evident in the calyces. In the urinary bladder a pronounced hæmorrhagic cystitis was present.

The immediate cause of death was toxæmia resulting from the bed sore and the pyelonephritis.

Histopathological Examination of the Central Nervous System.

The leptomeninges were infiltrated with polymorphonuclear leucocytes (some of which showed degenerative changes) together with occasional adventitial cells and a few lymphocytes. The meningitis varied in intensity and was patchy in distribution. It was most severe at the base of the brain and in the depths of the sulci. At some levels of the spinal cord, either it was absent, or it amounted to no more than a few scattered cells.

The principal alteration in the central nervous system was perivascular demyelination associated with loss or degeneration of axis cylinders, and with extraadventitial and perivascular infiltration. In sections stained by Weil's method, a moderate number of vessels were surrounded by zones of demyelination up to two or three times their diameter, occasionally more. Sometimes adjacent areas coalesced to form larger foci (Figure I). Many of these zones of demyelination were visible to the naked eye; in longitudinal sections of spinal cord they measured up to three millimetres in length (Figure II). Demyelination was complete except at the periphery of the zones; here the myelin sheaths showed fragmentation and ballooning. In these areas (Bielschowsky's method) only a few axis cylinders (always the thick type) were still present (Figure III). In many of these tortuosity, fragmentation and ballooning were apparent. In a few places, in sections stained by Anderson's Victoria Blue method, there was a mild increase in the number of glial fibres in the perivascular zones. In sections stained with hæmatoxylin and eosin the foci of demyelination appeared as eosinophilic areas infiltrated with polymorphic microglial cells, granular corpuscles and a few enlarged astrocytes; together, these cells formed cuffs of moderate extraadventitial infiltration (Figure IV). Perivascular infiltration was mild in degree and usually not more than one or two cells in thickness. In sections stained with Scharlach R, the granular corpuscles were packed with bright red lipoid granules (Figure V).

Distribution of Lesions.

Spinal Cord.—The foregoing lesions were distributed fairly evenly throughout the white matter of the thoracic, lumbar and sacral levels of the spinal cord; but the thoracic region was affected somewhat more severely than the remainder. (The cervical part of the cord was not available for examination.) The changes appeared in all three white columns and bore no apparent relationship to any of the tracts of the nervous system. Similar lesions were seen occasionally in the grey matter, almost always in areas immediately adjacent to the white matter.

Brain-Stem.—Areas of perivascular demyelination together with the associated changes were present in the brain-stem; but compared with those of the spinal cord they were of milder intensity and fewer in number. In the *medulla oblongata* lesions were found in the pyramids and *funiculus cuneatus*. (In this region also a nerve root showed partial demyelination.) The lesions in the pons were widely scattered.

Cerebellum and Cerebrum.—No lesions were present in the cerebellum and cerebrum.

DISCUSSION.

Clinically, the disease manifested itself as an ascending myelitis, characterized at one stage in the course of the illness by mild diminution in the amount of sensory loss and in the degree of paraplegia. Death eventually resulted from the toxæmia of a large bed sore and of pyelonephritis, associated with an apparently unsuspected pyogenic leptomeningitis. Only a few cases of myelitis following vaccination have been recorded; they include those of Peake,[4] Perritt and Carrell,[6] Mage,[9] Brockbank[7] and Armstrong.[8] Peake's patient had almost completely recovered when he was lost sight of at the end of three months. In the cases described by Perritt and Carrell and by Mage partial recovery of function occurred. In the remaining two cases there was no improvement, the anæsthesia remained at about the level of the umbilicus, and both legs were affected by complete flaccid paralysis. Of the cases reported, that of Mage bears most resemblance in its symptomatology to the present one. (His case is also of importance, in that it suggests that violent physical exertion may be a factor in increasing susceptibility to post-vaccinal encephalo-myelitis.)

The majority of cases of post-vaccinal encephalo-myelitis recorded have occurred in childhood and adolescence, probably because vaccination is usually performed at this period. The occurrence of the condition in middle age (in this case, at the age of forty-seven years) is extremely uncommon. Hekman[9] has recorded two cases, in a man aged sixty-three years and in a woman aged thirty-five years.

The usual incubation period varies from ten to thirteen days, its maximum incidence being on the twelfth. Cases have been recorded, however, within the limits of two to twenty-six days after vaccination. In the present instance the incubation period was sixteen days. This observation falls to support the statement of Hekman,[10] that the incubation period of post-vaccinal encephalo-myelitis after revaccination is shorter than that after primary vaccination.

In the present case the long incubation period and the occurrence of initial symptoms suggestive of "influenza" are unusual. Cases of disseminated encephalo-myelitis following "influenza" or respiratory infection have been reported by Greenfield,[11] by Grinker and Bassoe[13] and by Davison and Brock.[12] The possibility that my case is also one of these and that its advent after vaccination was purely coincidental cannot be entirely eliminated.

Post-vaccinal encephalo-myelitis occurs much less commonly after revaccination than after primary vaccination. Armstrong noted that two out of 71 American cases were stated to have followed a second vaccination. Of 51 cases of post-vaccinal encephalitis, Hamel[14] recorded that five resulted from revaccination. In three of these cases, however, there was no trace of the original vaccination scar, so that it is possible that the first vaccination did not "take". One of the seven cases described by Turnbull and McIntosh[15] followed revaccination; no scars of the first vaccination were detected at post-mortem examination. Authentic cases, however, have been reported by Rozendaal,[16] by Querido[17] and by Kokken.[18]

In general, the character of the pathological changes was similar to that described by Turnbull and McIntosh, by Van Bouwdijk Bastiaanse *et alii*,[19] by Bouman and Bok,[20] by Schürmann,[21] by McIntosh and Scarff,[22] by Van Bouwdijk Bastiaanse,[23] by Perdrau,[24] by Turnbull,[25] by Coyle and Hurst,[26] by Lucksch,[27] and by Kokken, Querido and others. The brunt of the pathological process was borne by the spinal cord; the brain-stem was only mildly involved, whilst the cerebrum was spared. It was only by virtue of the lesions in the brain-stem that I was entitled to call my case one of "encephalo-myelitis" rather than one of "myelitis".

The meningitis which sometimes occurs in association with post-vaccinal encephalo-myelitis is always mild in intensity, occurs mainly in relation to vessels, and is mononuclear in type. In the present case the meningitis was more severe, and the majority of cells consisted of polymorphonuclear leucocytes. This purulent meningitis almost certainly resulted from infection of the spinal subarachnoid space from the overlying bed sore.

The presence of subpial and subependymal lesions has led to the suggestion that the ætiological agent may be distributed by means of the cerebro-spinal fluid; the perivascular lesions have been attributed to spread of the causal factor through the walls of the vessels to the surrounding nervous parenchyma. However, since the perivascular spaces contain cerebro-spinal fluid, the perivascular lesions also may equally well be considered to support the theory of distribution of the ætiological agent by means of the fluid.

Turnbull and McIntosh first described the principal lesions as perivascular "softening". Later, Turnbull retracted this opinion in favour of the term "demyelination". The latter designation tends to minimize the fact that, as part of the pathological process, loss of axis cylinders also occurs. For that reason the former appellation, "softening", is to be preferred, provided it is used in the sense employed by Hassin.[28]

With regard to the ætiology of post-vaccinal encephalomyelitis, three hypotheses have been propounded: (i) that the condition is caused by the direct action of vaccinia virus on the central nervous system; (ii) that the disease results from some other virus or bacterium introduced with the vaccine virus, or from some virus lying latent in the tissues and activated by the vaccine virus; (iii) that the complication is an allergic one, due to a local anaphylactic reaction in the central nervous system.

The theory that the condition is *encephalitis lethargica* or poliomyelitis has been disproved. The various hypotheses have been discussed in detail by van Rooyen and Rhodes, and by Thompson. At the present time, in the absence of conclusive evidence, the question must remain an open one.

SUMMARY.

Sixteen days after revaccination against smallpox, a soldier, aged forty-seven years, complained of symptoms suggestive of "influenza". After a further eight days symptoms of ascending myelitis appeared, which resulted in a flaccid paraplegia associated with a large bed sore and pyelonephritis. Death occurred fifty-five days after the onset of the illness, and seventy-one days after vaccination.

Histopathological examination of the central nervous system revealed disseminated encephalo-myelitis, largely but not entirely confined to the spinal cord. The pathological changes included perivascular demyelination accompanied by destruction of axis cylinders, and extraadventitial and perivascular infiltration with polymorphic microglial cells and granular corpuscles.

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Reviews.

A NEW EDITION OF A TEXT-BOOK OF OBSTETRICS.

THE sixth edition of "The Queen Charlotte's Textbook of Obstetrics" has been improved by the addition of a chapter on post-natal care, by the revision of the chapter on radiology and obstetrics and by the inclusion of the classification of Caldwell and Moloy relating to pelvic contraction.[1] In this edition there are still some statements which require comment. In the section on the treatment of abortion, the statement is made that "the presence of an infected ovum with pyrexia . . . is always a definite indication for evacuating the uterus". We have always acted on the understanding that pyrexia in the absence of hæmorrhage is a contraindication to the emptying of the uterus and have obtained results which justify this attitude. In the discussion on ectopic gestation the statement is made that "the distinction of these (that is, the conditions resembling ectopic gestation) from ectopic gestation is, in some cases, almost impossible". This is perfectly true; but mention might be made of the value of posterior colpotomy in clearing up the doubt.

Traction with the finger in the mouth is advised for delayed descent of the after-coming head. This is much more likely to cause serious trauma than fingers placed on the maxillæ, by which just as much force can be exerted with no likelihood of damage.

For the shock caused by acute inversion of the uterus, the intravenous use of gum and saline solution is still recommended as being second in importance to blood transfusion. Surely the intravenous administration of serum is much more effective. Then, too, pressure on the apex of the inverted mass is still recommended for its replacement, whereas the advice given in regard to the replacing of any herniated tissue is much more likely to be successful: "replace first the part which came down last".

In regard to termination of pregnancy, it is noticed with approval that laminaria tents have given place as the principal means to dilatation and curettage during the first twelve weeks. In the treatment of both *placenta prævia* and accidental hæmorrhage, plugging of the vagina is advised as a method of induction of labour. We have been able to control hæmorrhage by this means, but have never succeeded in inducing labour by it.

It has been noticed that the importance of the Rh factor has been stressed in this edition.

In conclusion, this sixth edition is a worthy successor to its predecessors, and the fact that such a well-presented volume has been produced in the midst of hostilities reflects credit on the authors, publisher and printer. It is a book which is well suited to medical students and to general practitioners.

[1] "The Queen Charlotte's Textbook of Obstetrics", by Members of the Clinical Staff of the Hospital; Sixth Edition; 1943. London: J. and A. Churchill, Limited. 9¼" × 6¼", pp. 589. Price: 25s.

XUM

ILLUSTRATIONS TO THE ARTICLE BY DR. F. B. BYROM.

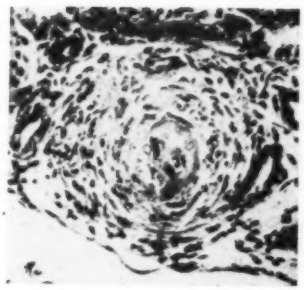

FIGURE I.
Acute necrotizing arteritis of a small renal artery from a hypertensive rat. The wall of the vessel is disrupted by fibrin and blood.

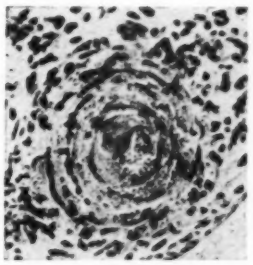

FIGURE II.
Acute necrotizing arteritis of a small pancreatic vessel from a human subject of malignant hypertension.

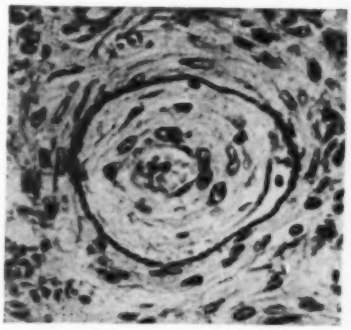

FIGURE III.
Endarteritis fibrosa of a small renal artery from a hypertensive rat. The lumen is constricted by a laminated thickening of the intima, limited externally by the thin black internal elastic lamella.

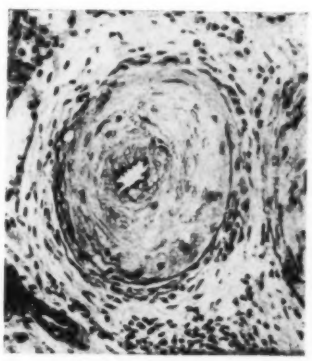

FIGURE IV.
Endarteritis fibrosa of a renal artery from a subject of malignant hypertension.

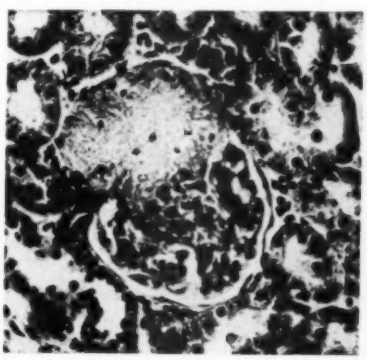

FIGURE V.
Acute focal necrosis of a glomerulus from a hypertensive rat.

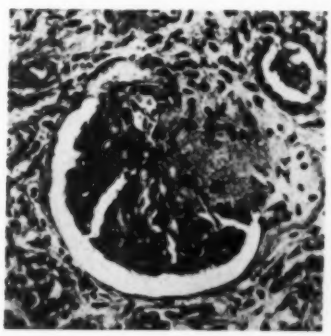

FIGURE VI.
Healed focal necrosis of a glomerulus from a subject of malignant hypertension.

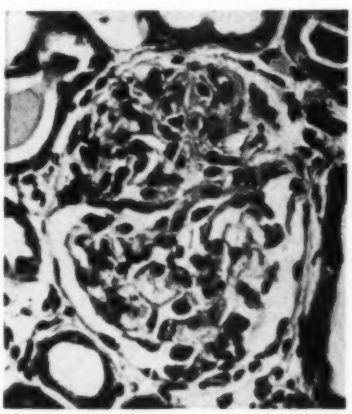

FIGURE VII.
Chronic glomerular lesion in a hypertensive rat. One-half of the tuft is hyalinized and adherent to the capsule.

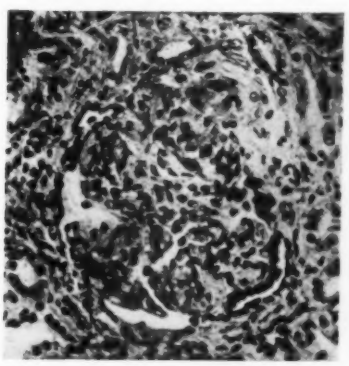

FIGURE VIII.
Chronic glomerular lesion in a case of malignant hypertension, showing extensive hyalinization and capsular adhesions.

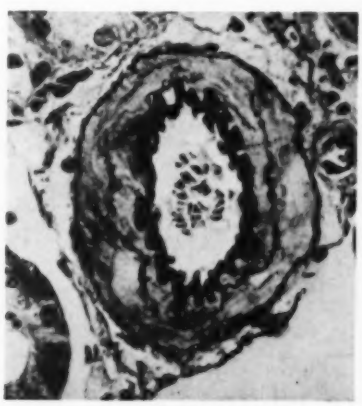

FIGURE IX.
Medical hypertrophy of a medium-sized renal artery from a hypertensive rat.

ILLUSTRATIONS TO THE ARTICLE BY DR. CHARLES SWAN.

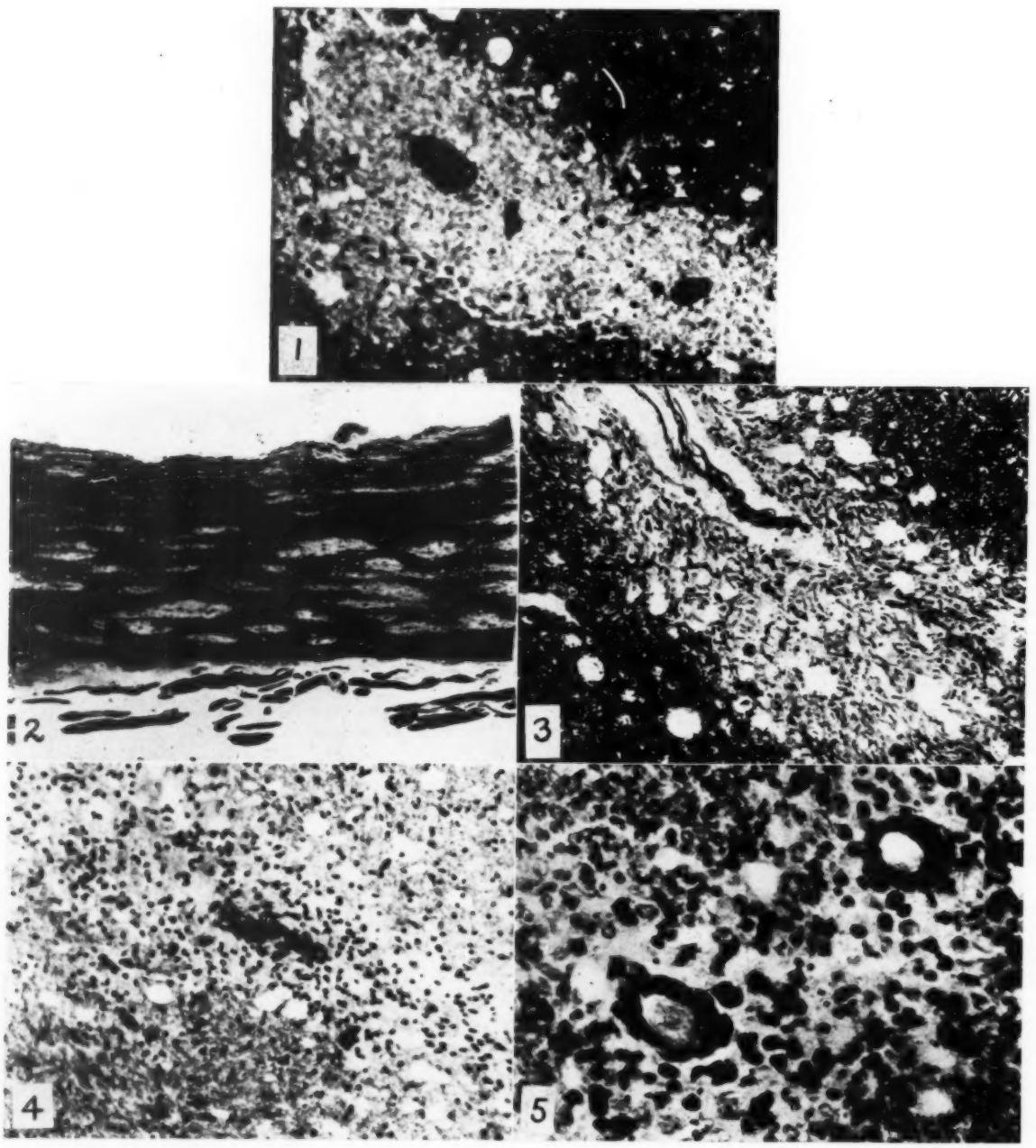

FIGURE I.—Spinal cord: perivascular demyelination. (Weil's method; × 140.) FIGURE II.—Spinal cord (longitudinal section): perivascular demyelination. (Weil's method; × 6.) FIGURE III.—Spinal cord: perivascular necrosis and degeneration of axis cylinders. (Bielschowsky's method; × 140.) FIGURE IV.—Spinal cord: perivascular and extraadventitial infiltration. Some post-mortem vacuolation. (Hæmatoxylin and eosin; × 140.) FIGURE V.—Spinal cord: perivascular and extraadventitial infiltration with lipoid-containing granular corpuscles. (Shariach R; × 208.)

The Medical Journal of Australia

SATURDAY, FEBRUARY 19, 1944.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

AN OLD LAMENT.

THERE are many subjects connected with medical practice, medical politics, medical literature and medical journalism which must be regarded as hardy annuals. Anyone who takes the trouble to look through old files of medical journals will consent to this statement. THE MEDICAL JOURNAL OF AUSTRALIA is in its thirtieth year, and during its lifetime occasions have arisen when certain well-discussed subjects have had to be brought forward again and again in the editorial columns. Those who sit on Branch councils will recall without difficulty discussions around the council table on some subject with which every Branch member should be familiar, but in regard to which a member is held to have wittingly or unwittingly transgressed. The question generally is how the sinner may be brought to see the error of his ways and determine to sin no more. Perhaps the matter is one concerning the profession in its relationship with some public body or with the State. A simple decision for the Council in such circumstances is to make a request that the subject should be discussed editorially in the journal. Sometimes, as events have shown, this is effective; sometimes the printed word does not come before those for whom it is intended. There are also certain folk, fit subjects for correction, who will never see that they need it—the message is always intended for the other fellow, "and quite right too". Even the best informed may falter and make a decision that is contrary to previously declared ideas. An example may be seen in a recent decision of no less a body than the Federal Council, which decided that uniform medical registration in Australia was not desirable, when for many years it had been one of the staunchest advocates of this necessary measure. From all this it is clear that the constant return to well traversed subjects, the everlasting reiteration of old ideas presented if possible in a new way, can easily be justified, for we have to do with those who don't know, those who know and forget, those who know and don't bother either because they are too lazy or because they are too self-satisfied, and those who know and allow their judgement to be warped from the crowding in of associated matters of importance and other demands on their time.

One of our hardiest annuals is the subject of medical certification; it comes to the fore more than any other, but in spite of all that could be written about it just now, it must stand over to give place to another not quite so often brought into prominence. The present time seems appropriate to make reference to some of the points that should be kept in mind by contributors, or would-be contributors, to this and other medical journals; and among these points special attention will be paid to bibliographic references and the vital importance of accuracy and attention to detail in their compilation. The conduct of this journal is complicated at present by two facts—much good material is waiting to be published, and owing to restrictions in the use of paper the accumulation of unpublished material becomes greater instead of less. One result of this congestion is that certain papers which in ordinary times would be printed without undue delay, do not at present see the light of day; the delay in other cases is disappointing to the author and a deprivation to the reader. From this it follows that articles accepted for publication must be shorn of all unnecessary embellishments and even of details that add little to the value of the subject matter. To discuss this aspect of the subject fully would call for reference to the diverse requirements and likings of the readers served by this journal and to the heterogeneity of material available to it; for our present purposes this is not needed. Such a great deal of the investigation carried out by workers in the laboratory and by clinicians at the bedside is founded on observations made by other workers and recorded in different parts of the world and so many of the opinions are based on the authority of other writers that the use of bibliographic references has become customary. This does not mean that the inclusion of many references to the literature is always necessary or desirable. References are of value when they serve to illuminate the argument of the author—as, for example, when he sets out differing views on the causation of a condition held by members of varying schools of thought that his own opinions may be stated in relation to them. As we have insisted on previous occasions, it is not necessary for a writer to quote an authority for every statement that he makes. To make the attempt is a trial to the author and more than wearying even to the willing reader. Very seldom also is it necessary to review the entire literature of a subject in the course of an article that is not stated in the title to be a review of the literature. An extensive bibliography is not necessarily an indication of an author's erudition. The value of a well-chosen and carefully checked set of references is greatest to someone who wishes to study for himself the subject on which an author has written. It is for this reason that this journal has followed the custom of including in all authors' references the full title of all articles. This is not done by all medical journals, but there can be no doubt that the references in journals adopting this style are more useful and more often used than those of journals in which the necessary space is not allowed for the fullest possible information. But while the information regarding each reference should be full and complete, it cannot be too strongly insisted that the

inclusion of references which an author has not himself consulted is dishonest unless he makes it quite clear that he has not done so. In these circumstances they are better omitted.

A final plea must be made for accuracy. Nothing is more tiresome to the student of any subject in medicine than to discover mistakes among references gathered in the literature and appended to an article. The results of inaccuracy do not end by irritating a reader. When once errors are found in a bibliography no one can blame the reader if he attributes to the author want of care in the making of observations set out in his paper and unreliability in the recording of them. The mistakes that are made in references by authors submitting papers for publication are almost unbelievable—an author's name will be incorrectly spelled; the names of one or more of those responsible for an article may be omitted; the initials may be confused; the title of the paper quoted may be that of a different article altogether; the year or volume number may be incorrectly stated (a very common error); even the wrong name may be given to a journal. An article is not infrequently quoted as coming from a certain journal when actually all that appears in that journal is an abstract taken from another publication. Every medical journal has a right to dictate the style that shall be followed in the setting out of references, and authors should try to conform to that style when they submit articles for publication. Editors cannot always discover errors in a set of references; when they have reason to suspect an author's accuracy faults will be rectified, but they, like the readers of journals, are sometimes deceived by appearances. Those who contribute articles to THE MEDICAL JOURNAL OF AUSTRALIA should be jealous of its reputation as a scientific publication and should therefore strive for accuracy in their contributions. They have an additional incentive in the fact that many Australian practitioners are working at some distance from medical libraries and are on that account more than usually dependent on what they read in their own journals.

Current Comment.

PATULIN AND ITS USE IN THE COMMON COLD.

SOME work of great interest has been carried out at the London School of Hygiene and Tropical Medicine on the use of a preparation known as patulin in the treatment of the common cold.[1] Some time ago a metabolic product of *Penicillium patulum* Bainier which had not previously been encountered at the laboratory of the London School was isolated and shown to have antibacterial properties. This product, which has been given the name patulin, has been identified as anhydro-3-hydroxymethylene-tetrahydro-γ-pyrone-2-carboxylic acid. Professor Harold Raistrick in an introduction to the lengthy account of the recent work explains that W. E. Gye, to whom the substance was sent for another purpose, tested it on himself, since he knew that it was equally effective against Gram-positive and Gram-negative organisms. At the time Gye was suffering from a severe common cold, and the results of the personal experiment were so encouraging that investigations were carried further and controlled experiments were planned and made. In addition to this experimental work it was necessary to investigate the optimum conditions for the formation of the substance and to settle its chemical structure. This work has been a well-planned piece of research, and its practical aspects should be brought to the notice of readers.

Patulin is described by J. H. Birkinshaw, S. E. Michael, Arthur Bracken and Harold Raistrick, who contribute a section on the biochemical and chemical aspects of the subject, as a colourless, beautifully crystalline substance with a melting point of 111° C. and the empirical formula $C_7H_6O_4$. It is obtained from filtrates of cultures of *Penicillium patulum* Bainier; more than one gramme of the pure substance may be obtained from a litre of culture filtrate. The pure substance completely inhibits the growth of *Staphylococcus aureus* at a concentration of one part in 64,000. It is soluble in water and in most of the commoner organic solvents except light petroleum. In the section of the report devoted to an account of the preliminary trial of patulin, W. E. Gye states that when he received the substance he was in the second stage of a severe common cold which had kept him indoors for two days. He prepared a watery solution of unknown strength (at least one part in a thousand) and douched the nasal passages thoroughly with it. The douching caused pain, but was followed within an hour by a clearing of the nasal passages; the douching was then repeated twice with a solution that was about one-tenth as strong as the original solution. The last douching was given at 9 o'clock p.m. A night of undisturbed rest followed and the next morning Gye was "completely well and back at work". Clearly after such a striking experience the matter had to be further investigated and this Gye proceeded to do. He first of all determined the strength of solution which could be used without accompanying pain. He found that the use of a solution of one part in 20,000 was practically painless and solutions of this strength buffered with phosphate at pH 6·0 were prepared and offered to medical and non-medical friends for trial. Some striking results were obtained and only one professional observer reported no improvement at all. Another medical man obtained alleviation of symptoms, but both maxillary antra filled with pus and had to be drained when no further trouble was experienced.

The results so far obtained justified the carrying out of controlled experiments, and for this purpose the cooperation of the Medical Director-General of the Navy was obtained and an investigation was carried out by Surgeon-Commander W. A. Hopkins at a naval establishment. Hopkins, who contributes a lengthy section to the report, first of all estimated the bacteriostatic power of the drug. He found that it was about equally bacteriostatic to Gram-positive and Gram-negative organisms. Compared with other mould products, patulin was found to differ from penicillin, gramicidin and citrinin in that it showed no selective differentiation between Gram-positive and Gram-negative organisms. Neither serum nor pus was found to have any effect on the bacteriostatic power. The in-vitro effect of patulin on the phagocytic activity of leucocytes was tested; it was unaffected by a solution of one part in 8,000, but was inhibited by a one in 2,000 solution. Hopkins selected for inclusion in the investigation persons who were suffering from "an acute or subacute rhinitis with or without pharyngitis, and with or without slight pyrexia and constitutional disturbance"—in other words from what the man in the street calls a cold in the head. The investigation was carried out in two parts, on two groups of persons. The first group comprised a series of persons, half of whom were treated with patulin and half with a control fluid. The second group comprised selected observers suffering from colds who were given supplies of patulin and were asked to keep careful notes of their progress. None of the patients in Group I knew whether they were being treated with patulin or with the control fluid, and in certain instances even those conducting the trials did not know which persons belonged to the treated group. Details of treatment and of the types of response cannot be described. It will suffice to state that of 95 treated persons 55 were cured and of 85 in the control group eight were cured. Improvement was assessed at the end of twenty-four and again at the end of forty-eight hours. If complete cure did not occur within forty-eight hours it was found to be unlikely that the patulin would

[1] *The Lancet*, November 20, 1943.

have any apparent effect in modifying the course of the cold. The cures of a large number of patients were complete in twenty-four hours. The failures were divided into two groups—one comprised those patients who did not manifest any kind of improvement, and the other those who manifested transitory improvement which was not maintained, or in whom complications developed. Sinusitis was a complication to which particular attention is drawn —Hopkins himself was one of those affected in this way. Group II comprised fourteen patients; ten made a rapid recovery, and of the remainder one felt better, but three noticed no improvement whatever. Apart from the complications no ill effects of the treatment occurred.

From the purely clinical side it should be noted that Hopkins excluded from his investigations any patients with any degree of sinusitis, tracheitis or laryngitis—conditions allowed to be present by Horder in his definition of a cold. The sinusitis that occurred as complications in Hopkins's patients may not have arisen after his treatment was commenced. *The Lancet* remarks that it has knowledge of another investigation, the results of which "were anything but encouraging". It will be interesting to compare this other investigation in detail with that reported from the London School of Hygiene and Tropical Medicine. At the same time it is important to note that, in the words of Raistrick, "since . . . it is desirable firmly to establish the value of the preparation and its complete freedom from danger when used as proposed, the material will not be released for general issue pending the completion of further large scale confirmatory trials". In these trials the use of healthy human volunteers may find a place.

PLASMA PROTEINS.

THE views held by physiologists and pathologists concerning the functions of the proteins of the plasma have undergone some curious vicissitudes. As the main solid matter in muscle, gland and connective tissue, apart from bone and tooth, is protein, the first and rather natural attitude was that the blood proteins were the chief purveyors of nutriment. When it became current doctrine that the active tissues of the body depended on crystalloids for energy and maintenance, a complete swing-over occurred and the plasma albumin and globulins were regarded as similar to the members of the House of Lords satirized by W. S. Gilbert—they did nothing in particular and did it very well. Physical chemistry, however, soon ascribed an important function to these colloids of the plasma in that they balance the osmotic pressure of the colloids of the cell. A tissue immersed in a so-called iso-osmotic saline solution invariably becomes œdematous, though owing to the massage of systole the onset of this condition in the living heart is postponed. This conception explained why protein should be found in several body fluids such as bile, pancreatic juice and saliva, but brought fresh complexities into the study of the cells of the lining membrane of the urinary tract which are in contact with a protein-free fluid. It was further recognized that proteins conferred on blood that viscosity which is necessary in maintaining the peripheral resistance adequate for systemic arterial pressure. The superiority of a protein-containing fluid over physiological saline solution in intravenous injection is so well known that a mere mention will suffice. In later years there has been a partial reversion to the idea that plasma protein can act directly as a nutriment. Experiment has shown convincingly that in protein starvation there is a steady fall in the plasma albumin, though little change is manifest in the globulins.[2] When food protein is administered in this state the rise in blood albumin accounts only for a small fraction of that ingested; obviously there is some equilibration between tissue protein and blood albumin.[2] It has long been a puzzle why, when fat can be stored in ample volume and a carbohydrate magazine can be developed in the form of glycogen, no apparent hoarding of protein takes place. Now through these protein-starvation experiments we learn that the tissues can in all verity accumulate protein and furnish substantial repayments to the blood when necessary. Another function of the plasma protein and particularly of the albumin which accounts for 80% of the osmotic pressure exerted by total colloids in the blood, is the maintenance of the blood volume. Most of our modern knowledge on this point is based on the pioneer work of Starling.[1]

Globulins are now recognized as complex and of varying types. In the beginning of this century there was a biochemical school which held that albumins and globulins were interchangeable and that the difference was mostly a matter of molecular volume due to loose aggregation and also to loose union with electrolytes. The present attitude is far removed from this. Antibodies and the four components of complement are now classified as globulins, and so this type of protein is now regarded as more concerned with defence than with nutriment.

Most interesting are the advances in the methods of separation and identification and estimation of the plasma proteins. In the old days the stock procedure was fractional salting-out with ammonium sulphate, magnesium sulphate, sodium sulphate or zinc sulphate. After this rather crude technique came the ultracentrifuge and then the very fruitful method of measuring the migration in an electric field. Albumins migrate most rapidly, then α-globulin, then β-globulin and then γ-globulin (the antibodies by the way are γ-globulins). There are other methods of attack, such as ref active index, specific gravity, viscosity, sedimentation rate of erythrocytes, cephalin flocculation, colloidal gold tests and, of course, the immunological reactions. It is curious to note that no use today is made of the measurement of rate of diffusion to which the Australian physicist William Sutherland first drew attention.[3] This technique demands no costly apparatus and gives results comparable with those yielded by the high-priced ultracentrifuge.[3]

TREATMENT OF CHEMICAL BURNS BY BUFFERED PHOSPHATE SOLUTION.

A PURELY theoretical suggestion has been put forward by Eduard Poser and Erwin Haas regarding the danger of using acids or alkalis in the treatment of burns produced by substances of opposite reaction.[4] It is pointed out that the 5% acetic acid usually applied to burns from alkalis has a hydrogen ion concentration well above the limits for safety when in contact with living tissue; on the other hand a 5% sodium bicarbonate solution, though deviating much less from the standard reaction of living matter, has sufficient alkalinity to be harmful. These authors recommend the use of a mixture of 70 grammes of acid potassium phosphate and 180 grammes of disodium hydrogen phosphate (Na_2HPO_4, 12 H_2O) in 850 cubic centimetres of water. The hydrogen ion concentration of this solution is that of blood and tissues, but the buffering power, at least in theory, is considerable, and so it could be employed in neutralizing the offending acid or alkali. It is claimed that whereas the treatment of these burns in the past demanded some chemical knowledge of the causative agent in order to choose the proper antidote, this phosphate solution can be applied to any acid or alkali which has accidentally come in contact with eyes or skin.

[1] A. A. Weech: "Significance of Albumin Fraction of Serum", *Bulletin of the New York Academy of Medicine*, Volume XV, 1939, page 63.

[2] S. C. Madden and G. H. Whipple: "Plasma Proteins: Their Source, Production and Utilisation", *Physiological Reviews*, Volume XX, 1940, page 194.

[1] E. H. Starling: "On Absorption of Fluids from Connective Tissue Spaces", *Journal of Physiology*, Volume XIX, 1896, page 312.

[2] W. Sutherland: "A Dynamical Theory of Diffusion for Non-Electrolytes and the Molecular Mass of Albumen", *Philosophical Magazine*, Volume IX, 1905, page 781.

[3] Charles A. Janeway: *New England Journal of Medicine*, November 11, 1943, page 751.

[4] *The Journal of the American Medical Association*, November 6, 1943.

XUM

Abstracts from Medical Literature.

DERMATOLOGY.

Epidermolysis Bullosa.

A. C. FRANKS AND M. I. J. DAVIS (*Archives of Dermatology and Syphilology*, May, 1943) state that *epidermolysis bullosa*, sometimes described as *acantholysis bullosa*, a somewhat rare dermatosis, is of considerable interest. The hereditary disease is uncommon in civilian practice. In military life, especially with the careful selection of the members of the armed forces, it is most rare. Recently, four soldiers were admitted to a general hospital complaining of this rare dermatosis. Two of these had the hereditary type and one the acquired type. The fourth had a rare hereditary type with bullæ limited to the feet. Cockayne described this type in the *British Journal of Dermatology* in 1938. No case of this type has previously appeared in the American literature. The authors give detailed reports of the four cases. The clinical and histological pictures are presented.

Combined Vaccine and Toxoid Therapy of Staphylococcic Infections of the Skin.

M. H. GOODMAN (*Archives of Dermatology and Syphilology*, May, 1943) states that in the laboratory animal staphylococcus antitoxin increases the resistance of the skin to the necrotizing power of staphylococcus toxin (anatoxin). In the common varieties of coccogenous dermatoses in which the staphylococcus plays a primary or secondary role, it has never been satisfactorily proved that the clinical and pathological picture can, in whole or in part, be accounted for by formation of toxin. The good results reported in the treatment of such infections by means of subcutaneous injections of increasing doses of staphylococcus toxoid have ordinarily been attributed to an augmented antitoxic titre in the blood. The author refers to the conflicting results obtained by other authors with the use of toxin and toxoid. Although injections of increasing doses usually augment antitoxic units in the blood, it is probable that the immune bodies often fail to reach the skin in sufficient quantity to neutralize the free toxin. Poor results might be due to a weakly antigenic toxoid. It is safe to assume that the common varieties of staphylogenous dermatoses, including pustular acne, are not dependent entirely on the action of toxin or the lack of production of antitoxin. It has sometimes been found that a patient with a good serological increase in staphylococcus antitoxin titre in response to injections of toxoid showed poor clinical results, whereas one with a poor serological response did well. Allergic hypersensitivity to the metabolic products of the staphylococcus undoubtedly plays a greater or lesser role in cutaneous infections due to this organism. It is understood that detoxified staphylococcus toxin (toxoid), as commonly prepared, contains many of the metabolic products of the organism. However, to assure a high content of these, capable of maximum effects, it was desirable to have available for clinical use a preparation which combined staphylococcus toxoid of high potency with a bacterial vaccine. The antigen employed in the author's study was described as a polyvalent staphylococcus vaccine combined with a standardized staphylococcus toxin, detoxified with formaldehyde to form a toxoid. All injections were given into the deltoid muscle, left and right alternatively. The initial dose was 0·1 cubic centimetre and the dose was increased by this amount at each treatment, which was given every fourth day until the patient received the tenth injection of one cubic centimetre. These injections were considered a full dose. The total number of patients treated and observed sufficiently to draw conclusions was 105; they suffered from a variety of conditions. All patients had some local reactions at the site of the initial injection, marked by tenderness, with or without erythema and extending over an area one to two inches in diameter. Subsequent injections produced much less reaction, even with repeated one cubic centimetre doses. Severe reactions, both local and constitutional, were observed in only two cases. By means of this desensitizing regimen it appeared that most of the patients were benefited and a great number obtained what may be justifiably considered a clinical cure.

Petroleum Dermatitis.

M. G. ROSENBAUM (*Archives of Dermatology and Syphilology*, August, 1943) states that petroleum produces erythemato-papular as well as papulopustular itching eruptions of the hands and forearms and thighs. In the follicles of the involved parts, especially on the dorsum of the fingers, small hard kernels of horn are formed, or in the presence of infection a follicular acne develops. The effect is totally different if petroleum comes in contact with the sensitive normally covered areas of the skin. On rare occasions there is bullous dermatitis. In 1929, Fellner reported a case of petroleum dermatitis in a fifty-four year old woman who had treated her sore throat by applying a petroleum soaked compress. Bullous dermatitis developed, which later spread over most of the trunk and the proximal half of the thighs. She died five days later. In 1935 Adams and Irby published a case in detail. The patient was a petroleum worker in whom a vesiculo-bullous dermatitis developed after these areas had been soaked with fluid from an oil well. Three Netherlands authors, Beck, Dwarshuis and van Kekem, reported three more cases. In Beck's case, that of a three year old boy, the dermatitis developed after contact with petroleum-soaked clothes. In the author's first case a worker in a glass factory stated that on the previous day he had been assigned to the department of glass cutting. In the course of his work he first rubbed the glass plate with petroleum and then held it with the edge against his abdomen, so that petroleum continually soaked his overalls, as he cut the glass with a diamond. On the evening of the same day he noticed itching and later a burning pain in the skin of the abdomen. Examination showed a round superficial blister in the right lower abdominal quadrant. The author's second case was that of a youth who went to bed without any signs of an eruption. The bed and straw mattress had been disinfected with petroleum the same day. The sheet was fresh and had not been disinfected. The next morning he awoke with rather violent itching on the left side of his chest, the side on which he was accustomed to sleep. On examination four hours later the author found inflammation on the left side of the chest which extended from the supraclavicular region almost to the nipples. There were hundreds of canary yellow vesicles, which contrasted with the bright red background. The blisters varied from the size of a pinhead to that of a plum and were mostly grouped. The blisters were strikingly flaccid and wrinkled when touched. In his summary the author states that cases of this type are apparently uncommon, as few reports have appeared in the literature. This rarity is due to the fact that the presence of three factors is necessary for the development of petroleum dermatitis: (*a*) the action of petroleum, (*b*) individual susceptibility, and (*c*) intense perspiration, friction or other mechanical irritation of the skin. The clinical picture of this disease is characterized by canary yellow blisters, extraordinary flaccidity of the unbroken vesicles, and a red, œdematous zone around the blisters.

Keratodermia Blenorrhagica.

A. GIRDWOOD FERGUSSON AND F. J. LEES (*The British Journal of Dermatology and Syphilis*, May, 1943) state that the ætiology of *keratodermia blenorrhagica* is still controversial. The disorder was first described by Vidal in 1893. In general, the popular theory would appear to be that it is one of the specific manifestations of "metastatic" gonorrhœa, and probably the sole cutaneous eruption that may be said to be a characteristic thereof. The authors quote Sutton, who states that a colleague, J. R. Campbell, has actually demonstrated Neisserian cocci in the skin lesions in a typical case. As regards the symptomatology and clinical picture of the condition, it may be described as a symmetrical eruption, composed of horny, conical nodules, pustules and crusts. While no site is exempt, the areas of predilection are the internal plantar margins and the dorsum of the great toe, the knees and palms being also, though less commonly, affected. There is a dirty yellowish epidermal thickening, often with "relief-map-like" projections, and on this account it is usually classed among the cutaneous hypertrophies. It is commonly associated with severe balanitis, apparently independent of the original genital inflammation. The authors give details of a patient who was admitted to a military hospital with a history of "sore eyes" of three weeks' duration. A few days later he began to complain of pain and swelling of the left ankle and knee joints and of a "discharge from the penis" and was transferred to the special treatment block. He was found to be suffering from an acute balanoposthitis, an acute interstitial keratitis, and arthritis of the left knee and ankle joints. He gave a history of exposure to venereal infection two months prior to admission, but gave no history of urethritis. No specific organisms could

be found in the subpreputial discharge, and the urethra, prostate and seminal vesicles appeared healthy. No reactions were obtained to the blood Wassermann and Kahn tests or the gonococcal complement-fixation test. In view of the above findings, he was then, eleven days after admission, admitted to the medical division. An eruption then began to appear, and when a few weeks later he was seen by one of the authors the typical clinical picture of a very generalized *keratodermia blenorrhagica* was present. Renewed efforts were made to locate and if possible eradicate an underlying focus. The deep adnexæ were still normal, and repeated massage thereof revealed only a few prostatic leucocytes and no organisms. On numerous occasions no culture was obtained from fluid from freshly arisen pustular lesions and the blood, too, proved sterile. In view of this the authors feel it is difficult to avoid suspecting that *keratodermia blenorrhagica* may well be another example of a typical cutaneous eruption, with a characteristic histopathological picture, which, however, may arise from various causes in different or perhaps in the same individuals. The authors conclude that blenorrhagic keratodermia would appear to be non-specific and ætiologically allied to such disorders as urticaria, *erythema nodosum* and *erythema multiforme*. The disease should, therefore, be classified, not among the hypertrophies, but among the exudative inflammatory disorders of the skin.

UROLOGY.

Prostatitis and Seminal Vesiculitis.

R. B. HENLINE (*The Journal of the American Medical Association*, November 6, 1943) states that a patient with infection of the prostate and seminal vesicles may present a clinical picture varying from that of an acutely ill patient to that of one who is unaware of a smouldering infection. The chronic infections are very common, so much so that Hinman of San Francisco estimates that about one-third of all adult males have infected prostates, though only a few of these infections are clinically obvious. The infections arise most frequently from a distant focus of infection or from some non-gonococcal infection in some part of the urinary tract. In a small percentage of cases they follow gonococcal infection. Urinary and genital symptoms frequently attract attention to the prostate, but these symptoms may be absent, and yet an infected prostate or vesicle may be causing trouble in a joint or elsewhere. However, quite often some referred pain occurs, and this is usually in the lower part of the back, around the pelvis somewhere, in the perineum or at any point in the sacral nerve centres of the lower extremities. The diagnosis is made by discovering tenderness, nodularity or bogginess on rectal palpation, and by the discovery of pus in the material expressed from the prostate, with sometimes a positive culture. The original focus of the prostatic infection is most often in the teeth or tonsils, less often in the alimentary tract or skin, and should be eliminated. In obstinate cases the clinician should make sure that reinfection of the prostate is not taking place from bacteria in the urine as a result of pyelonephritis of an obscure type. He must be sure to dilate the urethra while prostatic massage and sulphonamide therapy are being carried out; and any narrowings of the urethra or bladder neck should be eliminated.

Proliferative Lesions of the Urinary Tract.

W. C. STIRLING AND J. E. ASH (*Urologic and Cutaneous Review*, August, 1943) state that all the special or bizarre forms of chronic cystitis may be grouped under the term "proliferative cystitis". Similar lesions may affect the mucosa of the renal pelvis and ureter. Proliferative lesions of the urinary tract are initiated by chronic infection producing metaplasia of the epithelium. The subsequent picture depends on whether the change is to a squamous or a glandular type. The onset of proliferative disease is marked by a passage of blood, an occurrence which should always direct one to search for these special lesions. In the bladder cystic cystitis or glandular cystitis may initiate a malignant lesion. In lesions of the upper part of the urinary tract, several retrograde pyelo-ureterograms, with diminishing distension, may delineate the cysts of cystic pyelo-ureteritis. The treatment is repeated lavage of the renal pelvis with silver nitrate, dilatation of the ureters and fulguration of vesical cysts. The *Bacillus coli* is the most persistent offender in these conditions, and is attacked by various sulphonamides.

Ectopic Ureter in the Female.

B. J. ABESHOUSE (*Urologic and Cutaneous Review*, August, 1943) describes a personal case of ureteral ectopia, with the external opening situated in the uterus. The author has discovered only four other similar cases in the literature. The pathological embryology relevant to ectopic ureter is discussed. The cause may be (*a*) early abnormal fusion of the Wolffian duct with the Müllerian ducts or (*b*) opening of the ureter into Gärtner's duct, the persistent remnant of the Wolffian duct in the female, which subsequently becomes dilated and ruptures into the cervix, or, more commonly, into the vagina. The characteristic symptom of ectopic ureter in the female is diurnal and nocturnal incontinence, associated with periodic normal voiding. In the male, the chief symptoms are those associated with dilatation and infection of the ectopic ureter and the kidney above it. The diagnosis in the female is relatively simple because of the above characteristic history, and the accessibility of the ectopic ureter. In the male, the diagnosis is extremely difficult, and is seldom made clinically. The treatment is always surgical, and should be directed toward obtaining a permanent cure of the incontinence and complete eradication of infection. Conservative surgery is indicated when there is a normal kidney on each side or a congenital solitary kidney; the type of operation used is implantation of the ectopic ureter into the bladder by suprapubic extraperitoneal approach. In the case of an uninfected ectopic ureter draining the upper segment of a double kidney, ligation of the ectopic ureter in its abdominal portion through a suprapubic extraperitoneal approach affords an easy means of curing the incontinence by suppressing function in the upper renal segment. Nephrectomy or heminephrectomy is indicated in cases associated with dilatation and infection of the affected ureter and corresponding renal segment.

Urinary Complications of "Sulphadrug" Therapy.

R. W. BARNES AND G. K. KAWAICHI (*The Journal of Urology*, February, 1943) state that the most important factors influencing the formation of sulphonamide urinary concretions are: (*a*) concentration of the drug in the urine which may be influenced by decreasing the dose and increasing the fluid intake; (*b*) the degree of acetylation of the drug which cannot be influenced by extrinsic means; (*c*) urinary stasis which is overcome by establishing and maintaining free drainage; (*d*) the pH of the urine which may be adjusted; (*e*) body temperature which may be elevated. As the pH of the urine and the body temperature rise, so does the solubility of sulphonamide drugs in the urine. When the presence of crystals in the tubules, pelves or ureters is suspected, removal may be facilitated by local increase in temperature (short-wave diathermy) and renal pelvic lavage with hot sodium bicarbonate solution.

Vesical Diverticulum.

A CLINICAL study of a series of cases of diverticulum of the bladder associated with bladder neck obstruction has been made by P. Adams (*The Journal of Urology*, April, 1943). The large majority are treated quite successfully by conservative means, that is, without diverticulectomy. Treatment should be directed primarily to adequate removal of the obstruction. The results after perineal prostatectomy were excellent, although the diverticula were larger and more retentive than those in which transurethral resection was carried out. The mandatory indications for diverticulectomy are tumour or stone within the diverticulum, gross urinary retention which cannot be relieved by dilatation or resection of the diverticular orifice, and gross infection in a persistently retentive diverticulum. Proof of retention is obtained by making an aero-cystogram after filling the bladder with sodium iodide and draining off the iodide solution.

Vasitis Nodosa.

J. A. BENJAMIN, T. D. ROBERTSON AND J. G. CHEETHAM (*The Journal of Urology*, April, 1943) describe under the title *vasitis nodosa* a non-tuberculous nodular condition of the *vas deferens*, which is believed to be a clinical entity not previously described. In this case an associated staphylococcal vesiculoprostatitis was present. The lesions are about the size and consistency of a small glasshead on palpation, and are larger and more numerous near the epididymis. Pathologically, the vasal wall was the site of small round-cell infiltration, and in the muscular layer small spaces lined with epithelium were seen. Some contained spermatozoa. Possible ætiology is discussed—faulty development, infection, diverticula and cyst formation. The authors favour the theory of maldevelopment by the caudal group of mesonephric tubules.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on October 21, 1943, at Saint Vincent's Hospital, Darlinghurst. The meeting took the form of a number of clinical demonstrations by members of the honorary medical staff of the hospital. Part of this report was published in the issue of February 5, 1944.

Sinuses and Fistulæ after Appendicectomy.

DR. V. M. COPPLESON showed a female patient, aged twenty-nine years, who had been admitted to hospital on November 27, 1942; she had had a fæcal fistula and a discharging sinus in the right iliac fossa for two years. She had undergone an appendicectomy operation at another hospital in November, 1940. Three weeks later an abscess developed in the appendiceal incision. She was admitted to another hospital and remained there for three months, during which period she underwent two further operations. The patient then spent three or four weeks at a convalescent home; a discharge was still present in the wound. She was then admitted to yet another hospital in May, 1941, where she underwent two further operations and was given X-ray treatment; it was thought that the condition might be actinomycosis. Up till October, 1941, the discharge from the wound was only purulent matter; but from then on it consisted of pus and fæces. After receiving X-ray treatment, the patient spent four months at a convalescent home before being admitted to Saint Vincent's Hospital. At that time her bowels acted three or four times per day, partly through the fistula. She had lost three stone in weight in two years.

On examination, the patient was seen to be extremely emaciated. The right hip was flexed to a right angle, and an area of excoriation of the skin extended for six or eight inches around the wound (two long, deep, puckered scars). Operation was undertaken. The small bowel was divided near the ileo-caecal valve and anastomosed to the transverse colon. The fæcal discharge from the wound ceased, and the excoriation of the skin subsided. The flexed leg was straightened by extension. The patient was put in a bath; her condition improved considerably under treatment by massage and movement, and when she left hospital, she was able to walk with assistance. When she was examined three months later she had gained three stone in weight and was able to walk; but a slight discharge was still coming from the wound. Movements of the right hip were free.

Multiple Abdominal Hydatid Cysts.

Dr. Coppleson also showed a male patient, aged forty-six years, who had been admitted to hospital on September 10, 1943; he complained of heartburn and indigestion present for six or seven years, of headache present for one month and of vomiting of two weeks' duration. Twenty-four years previously he had undergone an operation for abdominal hydatid cysts, and had enjoyed good health until seven years prior to his admission to hospital, when he suffered from pneumonia. Since then he had had severe heartburn after meals; it had become worse during the last few months. The patient said that his indigestion was worse after spicy foods. He had lost ten pounds in weight in the last three months. The bowels were open when he took aperients and ate bulky food. He had no jaundice, though his complexion was sallow. No alteration had occurred in the colour of the stools.

On examination, a right upper abdominal scar was seen and a large mass was found in the right hypochondrium; it was not typically cystic, and no hydatid thrill was noticed. Operation was undertaken. Five small cysts were found in the omentum and completely removed. Three larger cysts were present attached to the posterior abdominal wall and the transverse colon; one of them was infected. These were opened and the endocyst was removed; swabbing with eusol was carried out and drainage was instituted. One large cyst with numerous daughter cysts was present in the left lobe of the liver; the endocyst was removed and drainage was instituted. A crescent-shaped cyst lying over the left lobe of the liver and in the region of the spleen was similarly treated. One small cyst lying in the pelvic pouch of the peritoneum was treated in the same way. The cavity was closed, three drainage tubes being left in position. At the time of the meeting the patient felt well, and was able to eat and enjoy all types of food; his wound was healing, and all the tubes had been removed.

Marjolin's Ulcer of the Scalp and Hand.

Dr. Coppleson's third patient was a male, aged forty years, who had had a tumour on his scalp for twelve months. At the age of two years, the patient had been burnt by a gas jet on the scalp and the left hand and behind the left knee. The burns healed and the patient had remained well until twelve months prior to his admission to hospital, when a small lump appeared on the scalp in the left occipital region. At the same time a "growth" developed on the dorsum of the left hand, the site of the old burn. Before being admitted to hospital the patient had been treated with radium at the out-patient department. One month before his admission a biopsy had been taken, and examination of the specimen had revealed carcinoma (Marjolin's ulcer).

Operation was undertaken on February 4. The carcinoma of the scalp was excised, tissue being removed down to the pericranium; a deep denuded area was left. Skin was grafted onto this area from the right thigh. Enlarged glands were dissected out from the neck. The pathological report on the excised tumour stated that it was a large raised tumour, and that on microscopic examination it was seen to be a squamous epithelioma, growing outwards rather than infiltrating inwards. Examination of sections of cervical glands revealed no metastases. The graft on the scalp took well, and within three months the deep depression had disappeared and the area was quite flat.

Osteomyelitis of the First Sacral Vertebra, with Rupture of an Abscess into the Spinal Canal.

Dr. Coppleson finally showed a male patient, aged twenty-seven years, who had been admitted to hospital on June 2, 1943. He had sustained an abrasion to his left wrist ten days previously. He returned to work four days later, the abrasion having healed; but immediately his left arm became swollen and painful, and he began to suffer from pain in the sacral area, of great intensity. The patient had not felt ill, and he had no headache or other pains. He had been constipated for three days. His temperature ranged from 100° F. to 103° F. and his pulse rate from 90 to 100 per minute; his respirations numbered 20 per minute.

On his admission to hospital, a blood examination gave the following information: the erythrocytes numbered 4,000,000 per cubic millimetre and the hæmoglobin value was 88%; the leucocytes numbered 14,000 per cubic millimetre, and neutrophile leucocytosis was present with a slight "shift to the left". Cultural examination of the blood produced no growth of organisms. An X-ray examination of the lumbar portion of the spine and the pelvis revealed no osseous lesion. Acute tenderness was present over the sacrum, but no evidence of any swelling was found. A rectal examination revealed no abnormality. The diagnosis was uncertain. The patient had a high temperature, and a course of treatment with sulphathiazole was instituted. About five days later the acute pain over the sacrum subsided, but the temperature was still raised and "swinging", and the patient appeared ill. This condition was followed soon afterwards by neck rigidity and symptoms of meningitis. Further X-ray examination failed to reveal any abnormality. Lumbar puncture was performed; no cerebro-spinal fluid was obtained, but at the third attempt thick yellowish pus was withdrawn. Examination of the pus revealed *Staphylococcus aureus*. The patient was then taken to the operating theatre and laminectomy was performed. The laminæ and some of the pedicles of the fourth and fifth lumbar vertebræ were removed. No pus was found in the spinal canal posteriorly, but when the dura was rotated pus escaped from the front of the spinal canal. The posterior bony portion of the sacral part of the canal was removed, the wound was packed with "Vaseline" gauze and a hip spica was applied. A blood transfusion was given. Blood examination on June 18 revealed hypochromic anæmia; the erythrocytes numbered 3,640,000 per cubic millimetre, the hæmoglobin value was 60%, the leucocytes numbered 19,900 per cubic millimetre and neutrophile leucocytosis was present. The patient's elevation of temperature slowly subsided; but on July 19 and August 2 respectively the leucocytes numbered 16,000 and 24,300 per cubic millimetre and the number of erythrocytes remained at 3,500,000 per cubic millimetre. The hæmoglobin value decreased from 60% to 50%. Iron was administered, the patient rapidly gained in health and strength, and the wound healed. On September 10 the plaster spica was changed. Dr. Coppleson said that recovery seemed to be satisfactory.

Rupture of the Spleen.

Delayed Rupture.

DR. J. L. HARDIE showed a male patient, aged twenty-three years, who had been admitted to hospital on January 29, 1943. He had sustained a crushing injury to his chest one week earlier, and on the day prior to his admission to Saint Vincent's Hospital he had left a suburban hospital at his own risk. That night he had felt severe pain in his left shoulder; this was followed within a few minutes by severe pain in the left hypochondrium, which soon spread to the whole abdomen and was accompanied by vomiting and diarrhœa.

On examination, the patient was pulseless, pale, sweating and semi-conscious, with sighing respirations. Signs of free fluid in the abdominal cavity were present, and tenderness was elicited in the left hypochondrium. The gravity of his condition precluded the carrying out of a comprehensive clinical examination. Within ten minutes of his arrival in the casualty department serum was being administered intravenously; this was soon followed by blood transfusion. The patient was taken to the operating theatre, and under local infiltration anæsthesia with a 0·5% solution of procaine, a left paramedian incision was made in the left upper quadrant of the abdomen. The peritoneal cavity contained a large quantity of blood, and the spleen was felt to be ruptured near the hilum. As pain was being felt at this stage, "Pentothal" was administered intravenously through the blood transfusion apparatus, and splenectomy was performed. One thousand cubic centimetres of blood from the peritoneal cavity were mixed with sodium citrate solution, filtered, and transfused during and immediately after the operation. Recovery was uneventful.

Traumatic Rupture: Multiple Injuries.

Dr. Hardie also showed a female patient, aged thirty-one years, who had been admitted to hospital on June 12, 1943, having been knocked down by a motor-car half an hour earlier. On examination, the patient was seen to be suffering severely from shock. The obvious lesions were (i) partial avulsion and laceration of the right fronto-parietal region of the scalp, (ii) lacerations to the buttocks, (iii) a fracture of the left fibula, (iv) a fracture of the left clavicle, and (v) a fracture of the left ulna. The systolic blood pressure was 70 millimetres of mercury and the diastolic pressure 40. No conclusive symptoms or signs of serious intraabdominal damage were present. Treatment for shock, including the intravenous administration of 2,000 cubic centimetres of serum, produced a poor response. Four hours after the patient's admission to hospital the hæmoglobin value was 30%; the hæmatocrit reading was 20. It was obvious that severe intraperitoneal hæmorrhage must have occurred. Under nitrous oxide, oxygen and ether anæsthesia operation was undertaken. The spleen was found to be lacerated and fragmental; no piece was larger than 4·0 centimetres in diameter. On this account the pedicle could not be brought into an accessible position. A lateral extension of the incision through the left rectus muscle, according to the technique of Rutherford Morrison, was necessary. *Débridement* of the scalp wound was carried out twenty-four hours later, under local anæsthesia. The patient made steady progress until one month later, when an infarct developed at the base of the left lung; great difficulty was experienced in differentiating it from a subphrenic abscess. One month after the patient had returned home obstructive jaundice supervened, and persisted for one month. At the time of the meeting she was in good health.

Autotransfusion.

Dr. Hardie then referred to the use of the patient's own blood for transfusion. He said that the patients whom he had just shown had both benefited by the administration of the large quantities of readily available blood in the peritoneal cavity. This blood was commonly thrown away, while the patient was in extreme need of such fluid. The apparatus for autotransfusion was simple and should be available in all hospitals, particularly in small country centres, where storing of blood was impracticable and donors were not readily available. Dr. Hardie went on to describe the method. He said that the blood was recovered from the peritoneal cavity by means of a small kidney dish or preferably a sucker with a sterile bottle in the circuit; he compared the apparatus with that used for tonsillectomy. One hundred cubic centimetres of sodium citrate solution (3·8%) were mixed with every 600 cubic centimetres of blood collected. The fluid was then filtered twice through ten layers of gauze on a funnel and given intravenously. The advantages of autotransfusion were the following: (i) the blood was readily available at the time of operation; Dr. Hardie instanced an emergency such as a ruptured ectopic pregnancy occurring in an outlying district; (ii) the blood was compatible and needed no matching; (iii) syphilis and malaria could not be transmitted; (iv) allergic reactions did not occur.

Stomach Lesions.

DR. V. J. KINSELLA showed two patients to illustrate the use of local anæsthesia for extensive gastric surgical procedures. The first patient suffered from extensive carcinoma of the stomach, involving the omentum and transverse colon; an almost complete gastrectomy and partial transverse colectomy had been carried out. The second patient suffered from a stenosing duodenal ulcer, with a stenosing anastomotic ulcer involving the stoma of a gastro-jejunostomy opening high up on the posterior surface of the stomach—too high to be of much use. An extensive gastrectomy was performed, together with a removal of part of the jejunum. Dr. Kinsella said that the outstanding feature in these cases was the remarkably good condition of the patients at the end of operation, with no sign of shock, and their absolutely smooth convalescence.

Buerger's Disease.

Dr. Kinsella then showed a patient suffering from Buerger's disease, to illustrate a highly satisfactory result from lumbar sympathectomy, although the patient's age was fifty-three years and X-ray examination revealed calcareous arteries. The patient had had gangrene of two toes of the left foot, treated conservatively, and was away from work for seven months. The disease had died down in this leg and a fairly good collateral circulation had developed. This self-limitation of the disease helped to confirm the diagnosis of Buerger's disease, as distinct from senile gangrene. Then the patient lost the tip of the second toe on the right leg, and then the first toe showed signs of ischæmia and a small patch of gangrene on the sole. The patient needed opiates at night and slept with his leg resting on a chair over the edge of the bed. Lumbar sympathectomy was performed on the right side. The result was the immediate loss of the severe "gangrene" pain and the rapid healing of the two toes affected; the patient was able to travel to the meeting by public conveyance and to ask for permission to return to work, six weeks after his operation. His left foot still felt warm and he used it at night to keep the right foot warm.[1]

Buerger's Disease and Tonsillitis.

Dr. Kinsella showed another patient, aged fifty-eight years, who had suffered from intermittent claudication for six months, and after walking ten times up and down the hospital veranda he had to sit down. An unusual and striking feature was the marble-like pallor, involving the foot and leg up to the knee, which came on after the patient had been walking. Examination revealed no additional abnormality, other than arterial calcification and grossly infected tonsils. Dr. Ramsay Beavis removed the tonsils. Two weeks after this operation the patient could walk fifty times up and down the veranda without pain, the pallor had disappeared, and he requested to be allowed to return to work. At the time of the meeting only slight disorder of the cutaneous vascular reactions could be detected. Dr. Kinsella said that an infective focus was a usual accompaniment of thrombophlebitis, and was probably an important ætiological factor. It could easily be a factor aggravating endarteritis. The patient was still under observation, and was to return for sympathectomy if his disability recurred.

Curious Behaviour of Infected Hand and Henry's Approach to the Ulnar Synovial Sheath.

Dr. Kinsella finally showed a patient suffering from suppurative teno-synovitis due to a streptococcal infection following a wound to the thumb. The radial synovial sheath became infected and the infection crossed to the ulnar sheath. The following points were of interest: (a) The sheath originally infected cleared up under conservative treatment (rest, elevation, the application of heat, and the use of sulphanilamide); but infection persisted in the sheath secondarily infected. (b) To evacuate the pus from the ulnar sheath, Henry's approach was used, through the medial border of the hypothenar eminence. Dr. Kinsella said that

[1] One week after the meeting, the patient had been back at work for one week and his feet were standing the strain well. He was the oldest patient whose case Dr. Kinsella had seen recorded to show good results from sympathectomy.

this approach was preferable to Kanavel's, because it inflicted much less trauma on the hand, it did not cross skin flexion creases, and it did not endanger volar digital nerves. The approach was ample and the results in the case under discussion were good. The patient had almost full movement in all fingers except the fifth, which already had a considerable degree of movement five weeks after operation.

NOTICE.

THE annual general meeting of the Section of Preventive Medicine of the New South Wales Branch of the British Medical Association will be held on Thursday, February 24, 1944, at 5 p.m., in the Board Room, fourth floor, Department of Public Health, 52, Bridge Street, Sydney. All members and intending members are invited to be present.

Correspondence.

THE FUTURE OF MEDICAL PRACTICE.

SIR: Churchill and Roosevelt have given us the four freedoms of the Atlantic Charter. I suggest that we might adopt a medical charter—the five freedoms:

1. Free choice of doctor and of patient.
2. Freedom from bureaucratic control of our practices.
3. Freedom of sale and purchase of our practices.
4. Freedom of domicile, for it has been largely forgotten that under a nationalized medical service doctors will have to go where they are ordered to go.
5. Freedom of our ancient Hippocratic tradition to be the trusted and confidential advisers of our patients, uninfluenced by any consideration other than the health and welfare of those whom we are privileged to serve.

Yours, etc.,

ARTHUR D'OMBRAIN.

Bank Chambers,
17, Bolton Street,
Newcastle,
New South Wales.
January 24, 1944.

SIR: To one returning from the political peace of active service to the struggle for existence of civil life, where apparently "all are for the party and none is for the State", it seems that a great many of the cross-purposes involved in discussions on this subject are actuated by fear. The fear of having something forced upon us which we do not think is right. But can anything be forced upon a free people determined to remain free? Surely it all depends on the degree of determination! So why this fear? Is the profession as a whole too exhausted by work under the present system, or just too apathetic to put up a successful fight for what it believes to be right? Or—nasty thought—so divided that members are unable to agree among themselves as to a basis for carrying on their work for humanity?

It seems to me that discussions might well boil down to the consideration of three facts:

1. That some change in the present system of medical practice in Australia is not only inevitable but desirable.

2. That any new scheme should and could be conducted by doctors themselves—by a council of men and women nominated and elected by members for their integrity of character, experience and executive ability. Such a council would have to include probably a government representative and certainly an actuary, but would need to be predominately professional.

3. That a scheme satisfactory to all has yet to be worked out.

1. That some change is inevitable is apparent from the record of this Government for getting things done. As to the desirability of some change of system, in the interests of patients and doctors, anyone having doubts would be well advised to undertake a week's locum in an industrial suburb.

2. Surely many of the objections to an organized scheme would disappear if doctors could be sure of working under an authority nominated and elected by themselves! The bogy of lay control could be flattened out once and for all by the formation of the body outlined above. The way for the creation of such a body could be opened by asking each member, of course, including those "O.A.S.", to sign a declaration to the effect that, in the event of a compulsory scheme being introduced, he or she would not accept service except under such an authority. Personally I think the number of "blacklegs" would be small; anyhow, it would be well to know who they are.

3. Such an authority when elected could proceed to the formulation of a scheme based first on our Hippocratic oath, and secondly on the need to provide for members the wherewithal to educate their families and enjoy at any rate as much leisure as their patients. Not a scheme to enable the commercial-minded to make fortunes out of human ills. Such a plan could embody private practice for some and a salaried service for others. A great deal of work has already been done, and members have ample opportunity of expressing their views as to details. When completed, the scheme could be submitted by referendum to members, and the council would be in a position to say to the Government, in language it would understand: "Here is our plan; take it or leave it; we can count on the loyalty of our members."

Yours, etc.,

MARY THORNTON.

Warrandyte,
Victoria,
January 18, 1944.

TOURNIQUETS: STRANGULATOR AND PRESSURE POINT.

SIR: Would somebody please help me? I am mystified by the continued preference in first-aid works for the use of the pad over the pressure point with constriction, and would be glad to know what are the alleged advantages (over the simple constricting band or strangulator), having especial regard to the insecurity of the pad over the vessel and the danger of venous congestion with even increased hæmorrhage if it slips.

I shall be grateful to be instructed on this point, and ask only that the information be reasoned; if it could also be the result of practical experience, it would be still more appreciated.

While familiar with the control of hæmorrhage in deliberate limb surgery, I have also to admit that my own experience in the early treatment of urgent hæmorrhage has been almost entirely limited to removing tourniquets [*sic*] already applied: in that field it has not been negligible and has met with marked success. There are, of course, some wounds whose natural coagulant powers have withstood even the tourniquet, and such have to be taken into account in considering lives "saved" by such means.

Yours, etc.,

C. C. MCKELLAR.

"Harley",
143, Macquarie Street,
Sydney.
January 26, 1944.

THE ANTISEPTIC PRINCIPLE.

SIR: "Nature and Nature's laws lay hid in night. God said, 'Let Newton be', and all was light." In this way principles are born. Principles shed light all around, and wherever that light is obscured error leads the way. Lister discovered the antiseptic principle which established the safe way, saying that however much the method which he used may come to vary, the principle itself will ever be that which shall guide the practice of surgery. In saying this, Lister was most emphatic; he had discovered a truth and called it a principle. My complaint is that I can find no evidence of the recognition of this guiding principle in medical practice today. It is a long way back to the time when the departure from it was made. I blame von Bergmann for it (another German atrocity), although it was only in part that he neglected it, and that was when he introduced the aseptic method. His followers did not fully grasp the limitations imposed within which the principle was preserved and this neglect made the aseptic system (?) the failure it has proved to be. I do not suppose that any of our practising surgeons have read Schimmelbusch's exposition of the Bergmann method; in it they will find confirmation of what I say, namely, that all signs of the principle were dissipated in application.

Yet how long it held sway—until World War I. Now a new vogue has set in. Antiseptics spurned are now in favour with the addition of new varieties, but still no sign of a guiding principle. Now, what is this very elusive principle? I suspect that when the aseptic method was embraced so readily it was infected by the bug of obtuseness so common and endemic in the German mentality; our principle so obvious at our feet remained unseen. Lister, having satisfied himself of the soundness of his principle with very crude reagents, proceeded with a search for the ideal antiseptic, not so much to kill germs in a wound, but rather to protect the wound from infection secondarily. He concluded that it was not necessary to kill infection in a wound and even declared that this could not be done. He said he could depend on the self-cleansing properties of the tissues to destroy the invaders, having blockaded them with his antiseptic dressing. He argued that an enemy so placed could have no chance of survival against the unlimited defenders, Nature's way of providing for repair of injuries. "The vital forces of the body organise themselves at once to heal a wound." Lister was right in concluding that it would be impossible to kill wound infection *in situ*; so far, it has not been accomplished, bacteriostasis being its nearest approach. That, in itself, though very helpful, is not enough. We must still stick to the principle to get results consistently successful. The means at our disposal are legion, such as would delight Lister. Now I hear that the mere stuffing of wounds with the newest of the new in antiseptics is not enough; alternatively, the attack is being made through the blood stream and orally. In this way we invite risks such as Lister would never take; they are methods involving no strain on the intelligence and are devoid of any principle; they may even be described as shots in the dark. Five bulls and a centre is good shooting, but we want the possible. With the principle we can attain it. I must be short. The light, I hope is good, and as it shineth in the darkness, I trust the result will not be that the darkness still comprehendeth it not.

Yours, etc.,

A. C. F. HALFORD.

Brisbane,
February 9, 1944.

BLOOD SERUM IN THE TREATMENT OF BURNS AND WOUNDS.

SIR: Two years ago a letter by me appeared in THE MEDICAL JOURNAL OF AUSTRALIA on the treatment of burns by human blood serum. According to the local daily Press, human blood serum is being used extensively in both America and Russia for burns and wounds. There is little doubt that serum is just as superior to crystalloid solutions when used externally as when used internally. I have been treating burns and wounds with fresh blood serum and sulphanilamide powder for two and a half years and have been gratified with the results.

After cleaning up the burns and wounds meticulously I apply sulphanilamide powder. The serum is next poured on and gauze packs applied. The application of serum can be made over the gauze at frequent intervals. The final result is that one obtains a pool of serum with sulphanilamide in concentrated solution. It has been proved by pathologists that tannic acid has a deleterious action on the dermis and occasionally causes fatal hepatitis. Unfortunately I have been working alone on this new method of treating burns and have had no controls to judge its efficacy. From my small series of cases, however, I consider it a good method. It complies with the rule: *"Primum non nocere."*

Yours, etc.,

F. W. SIMPSON.

Perth,
Western Australia,
January 20, 1944.

A NEW TREATMENT FOR THYREOTOXICOSIS.

SIR: In the issue of January 29 under "current comment" a rather laudatory account was given on the use of thiourea and thiouracil in the treatment of thyreotoxicosis following on brief articles by E. B. Astwood who reported three cases and H. P. Himsworth who reported six cases.

Unfortunately no mention was made of the case in Astwood's series who developed a severe agranulocytosis, nor is any warning given as to other reactions which must be looked for in some cases. Astwood is mentioned as regarding his studies as preliminary only, but it is rather a pity that both investigators reported such a small series of cases.

Work is being carried out in Sydney by several men using thiourea, as this is the safer of the two drugs mentioned, and a word of warning to the profession at large may be advisable at this stage. Until such time as a series of cases has been fully checked under conditions where facilities are available for regular basal metabolic rate estimation, blood cholesterol and leucocyte counts along with four-hour charts and expert nursing attention, and an analysis of the types of case and results achieved can be published, it would be courting possible disaster for thiourea to be used by the profession at large.

Although I have had some five months' experience with thiourea in fifteen cases, I do not consider the series large enough to report as yet, nor can one evaluate results until at least six months have elapsed. All one can say at present is that results to date justify further experimentation by competent observers with full hospital facilities available, but the drug is by no means a cure-all, nor is its use unattended with risk.

Yours, etc.,

HUGH R. G. POATE.

225 Macquarie Street,
Sydney,
February 9, 1944.

LIQUOR REFORM.

SIR: I think that the decision of the Queensland Branch of the British Medical Association to openly support liquor reform—as published in THE MEDICAL JOURNAL OF AUSTRALIA of January 15—is the most wonderful thing I have seen in the pages of the journal.

May I be permitted to advocate that all local associations in other States take the matter up and press it upon their councils for similar action?

Further than that, this action but points the way to action on other fronts whereby doctors generally, acting collectively through their association, the British Medical Association, will see it as their duty to take a larger and larger part in all reforms which bear directly or indirectly upon the health and welfare of the community.

Lastly, should it be held that the Memorandum of Articles of Association of the association prevent such action, then I here foreshadow the necessary amendments.

Yours, etc.,

C. C. McKELLAR.

143, Macquarie Street,
Sydney,
February 9, 1944.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 29, of February 10, 1944.

NAVAL FORCES OF THE COMMONWEALTH.

Permanent Naval Forces of the Commonwealth (Sea-Going Forces).

Emergency List.

Termination of Appointment.—The appointment of Surgeon Lieutenant Leo John Harrison for temporary service is terminated, dated 23rd August, 1943.

Citizen Naval Forces of the Commonwealth.

Royal Australian Naval Volunteer Reserve.

Appointment.—Robert Andrew Du Val, D.S.C. (ex-Surgeon Lieutenant, Royal Naval Volunteer Reserve) is appointed Surgeon Lieutenant, with seniority in rank of 27th November, 1939, dated 8th December, 1943.

DECORATIONS.

THE name of Captain (Temporary Major) Reginald Neville Cudmore Bickford, A.A.M.C., has been mentioned in dispatches in recognition of gallant and distinguished service in the South-Western Pacific Area. Captain Bickford's name was omitted from the list supplied to this office and published in the issue of February 5, 1944.

A Correction.

In the issue of February 5, 1944, it was stated in error that Brigadier F. K. Norris, Lieutenant-Colonel A. F. Hobson, Lieutenant-Colonel E. C. Palmer and Captain J. A. M. Shera had, in addition to other decorations, received the British Empire Medal. The error is regretted. The British Empire Medal is an award given to "other rank personnel".

CASUALTIES.

ACCORDING to the casualty list received on February 16, 1944, Captain D. C. Whitfeld, A.A.M.C., who was previously reported missing, is now reported to have been drowned accidentally.

Medical Prizes.

THE STAWELL PRIZE, 1943.

THE trustees, acting on the recommendation of the appointed examiners, have awarded the Stawell Prize for 1943 to VX15158, Lieutenant-Colonel A. J. M. Sinclair, 114th Australian General Hospital, Australia. The subject for 1943 was "Psychiatric Aspects of the Present War", and the examiners in their report stated: "Among the essays submitted were several of very great merit."

Notice.

A CLINICAL AFTERNOON has been arranged by the Department of Mental Hospitals of New South Wales, and will be held at the Mental Hospital, Parramatta, on March 3, 1944, at 2.30 o'clock p.m. The programme will include demonstrations of the following conditions: Huntington's chorea with full family history; virilism with radiographs of skull and suprarenal bodies; abnormal breast hypertrophy; endocrine disorders; selected criminal cases; neurological disorders; X-ray film demonstration. An invitation to be present is extended to all members of the British Medical Association.

Nominations and Elections.

THE undermentioned have been elected as members of the New South Wales Branch of the British Medical Association:

Byrne, Ian Donald, M.B., B.S., 1943 (Univ. Sydney), Balmain and District Hospital, Booth Street, Balmain.

Cambourn, Paul, M.B., B.S., 1943 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Carroll, John Edward, M.B., B.S., 1943 (Univ. Sydney), "Bryn-Mawr", Bangalla Street, Warrawee.

Craven, Richard Allan, M.B., B.S., 1943 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.

Gillogley, Jack Francis, M.B., B.S., 1941 (Univ. Sydney), 60, King Street, Ashbury.

Hill, Kenneth Hamilton, M.B., B.S., 1939 (Univ. Sydney), 2, Victoria Street, Strathfield.

Kiely, Roger John, M.B., 1941 (Univ. Sydney), 26, Crescent Street, Haberfield.

Ross, Edgar Hughan, M.B., B.S., 1940 (Univ. Sydney), NX116468, Captain E. H. Ross, R.M.O., H.Q., R.A.E., 12 Australian Division, Australia.

Rothfield, Raymond David, M.B., B.S., 1943 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Shirley, Anthony David, M.B., B.S., 1941 (Univ. Sydney), Captain A. D. Shirley, 11 Australian Field Ambulance, Australia.

Vickers, Thomas Harold, M.B., 1942 (Univ. Sydney), Sydney Hospital, Sydney.

Books Received.

"A Handbook for the Identification of Insects of Medical Importance", by John Smart, Ph.D., with chapters on fleas by Dr. Karl Jordan, F.R.S., and on Arachnids by R. J. Whittick, B.Sc.; 1943. London: Printed by order of the Trustees of the British Museum. 9¾" × 7¼", pp. 291, with many illustrations, some coloured. Price: 15s.

"The Surgery of Repair: Injuries and Burns", by Squadron Leader D. N. Matthews, R.A.F.V.R., M.A., M.D., M.Ch. (Cantab), F.R.C.S. (England); 1943. London: Macmillan and Company, Limited. 8" × 5¼", pp. 398, with many illustrations, some in colour. Price: 45s. net.

Diary for the Month.

FEB. 22.—New South Wales Branch, B.M.A.: Ethics Committee.
FEB. 23.—Victorian Branch, B.M.A.: Council Meeting.
FEB. 25.—Queensland Branch, B.M.A.: Council Meeting.
FEB. 26.—Tasmanian Branch, B.M.A.: Annual Meeting.
MAR. 1.—Victorian Branch, B.M.A.: Branch Meeting.
MAR. 1.—Western Australian Branch, B.M.A.: Council Meeting.
MAR. 2.—New South Wales Branch, B.M.A.: Special Groups Committee.
MAR. 3.—Queensland Branch, B.M.A.: Branch Meeting.
MAR. 3.—Victorian Branch, B.M.A.: Legislative Subcommittee.
MAR. 7.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
MAR. 7.—New South Wales Branch, B.M.A.: Organization and Science Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

Editorial Notices.

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WHEAT, FLOUR AND BREAD, WITH SPECIAL REFERENCE TO ENRICHED FLOUR.[1]

By R. A. BOTTOMLEY, M.Sc., A.A.C.I.,
Melbourne.

IT is well known that upon the subjects of wheat, flour and bread opinions are many and varied. The farmer, economist, politician, processor, dietitian, doctor, consumer and so on, all have their different points of view. But of all these it is the opinion of the general public, the consumer, which is of the greatest practical importance. It may not be the best-founded opinion, but in normal times it is the deciding factor. However, it is not proposed to discuss the values of these various more or less well-informed opinions, but rather to present from the point of view of the cereal chemist a review of recent developments.

Wheat is the largest of all world grain crops, yielding about 145,000,000 tons per year, and from earliest times it has commanded a leading place as food for man and beast. The grain is not a true seed, but is a fruit containing one seed, in which the fruit wall (pericarp) is fused to the seed coat (testa). Under the microscope the pericarp is seen to consist of four distinct layers of differently shaped cells which cover the testa, making five cell layers in all which completely surround the remainder of the seed—that is, the endosperm and embryo or germ. Beneath the testa a fine, transparent layer of cells called the hyaline layer and a single layer of relatively large cells packed with protein, the aleurone cells, surround the endosperm and slightly overlap the germ.

The composition of pure endosperm, germ and bran will depend upon a number of factors, the most important of which are probably the variety of wheat and the climatic conditions under which it was grown. Fleurent[1] has recorded the proportions of pure endosperm, germ and bran to be approximately 85%, 2% and 13% by weight respectively, whilst Ferrari[2] has stated that the proportion of bran may vary from 17% to 23% of the grain. From the figures reported for pure bran by Moran and Pace[3] and from analyses made by the writer, the composition of these parts has been estimated to be as shown in Table I.

In view of the large number of varieties of wheat and of the different climatic and soil conditions under which they are grown, it is not surprising to find considerable variations in the composition of the grain. Even for Victorian "fair average quality" wheat, it is not unusual to find a 100% variation in protein content or a 300% variation in enzyme activity in any one season. The bulk of the crop, however, falls within narrower limits, and the analysis of an average sample of wheat is shown in the following tabulation:

Moisture	11·0%
Protein	11·0%
Starch (by difference)	70·0%
Crude fat	2·0%
Crude fibre	2·5%
Sugar	2·0%
Ash	1·5%

Wheaten Flour.

Wheaten flour is understood to be that portion of the endosperm recovered by the milling process. Briefly, the object of this process is to remove as completely as possible the bran and germ from the endosperm, at the same time grinding the endosperm to fine particles without excessive rupturing of the starch granules. Although milling has reached a high state of efficiency, only from 72% to 75% of the cleaned grain is obtained as flour under normal conditions; that is, about 85% of the original endosperm is recovered. Since modern milling is what is known as a gradual reduction process, flour is produced at several points within the mill. These types of flour, or more technically "flour streams", can be combined in various ways to make a series of finished varieties of flour

[1] Read at a meeting of the Victorian Dietetic Association on October 4, 1943.